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ELECTROPHRENIC RESPIRATION IN ACUTE BULBAR POLIOMYELITIS

Its Use in Management of Respiratory Irregularities

STANLEY J. SARNOFF, M.D.
JAMES V. MALONEY Jr., M.D.
L. CHARLOTTE SARNOFF
BENJAMIN G. FERRIS Jr., M.D.
and
JAMES L. WHITTENBERGER, M.D.
Boston

Acute bulbar poliomyelitis is not infrequently complicated by involvement of the center which drives and coordinates respiration. Such a defect is occasionally severe enough to interfere with adequate ventilation, even though the peripheral neuromyal respiratory mechanism may be spared by the disease. The difficulties resulting from involvement of the respiratory center are generally thought to be of two types, (*a*) grossly irregular respiratory rhythm and depth and (*b*) lack of coordination of the muscles of respiration. These difficulties, when severe enough, reduce the respiratory exchange to a critical level and result in sufficient hypoxia to intensify the pathologic conditions already present.

Attempts to manage this type of patient in the tank type respirator of Drinker and Shaw [1] are generally thought to be ineffective when involvement of the respiratory center is severe. This is largely because of the inability to substitute the respirator's rhythm for the patient's grossly irregular "respiratory fibrillation." It has therefore become general practice not to place such a patient in a tank respirator since use of it may increase the respiratory difficulty. Supportive therapy, with painstaking attention to maintaining an unobstructed airway, has remained the cardinal principle in the management of this form of the disease.

Two further considerations have intensified interest in the management of bulbar poliomyelitis. First, the death rate is significantly higher than in the spinal form of the disease. Second, it is generally thought that recovery from bulbar poliomyelitis is usually more nearly complete and more likely to leave a competent person than is recovery from a correspondingly severe case of spinal poliomyelitis. Previous attempts to use the tank respirator in the bulbar form of the disease have depended on either large doses of curare or the use of more forceful tank pressure gradients than those commonly employed. This article deals with the use of the electrophrenic respirator in the study and treatment of patients with respiratory irregularities due to the bulbar form of poliomyelitis.[2]

Although phrenic stimulation has not been used previously in bulbar poliomyelitis, artificial respiration by electrical stimulation is not entirely new.[3] In previous investigations it was demonstrated that, by rhythmic application of an electrical potential to one phrenic nerve, it is possible to produce adequate ventilation in the cat, rat, dog, rabbit, monkey and man.[4] The rate and depth of respiration are readily controlled within satisfactorily wide limits. More recently it has been found feasible to produce electrophrenic respiration in man by external stimulation over the motor point of a single phrenic nerve.[5] Such stimulation can be sharply localized to the phrenic nerve. It was also found, by differential bronchospirometry in 7 patients during electrophrenic respiration, that aeration of the lung on the unstimulated side is only slightly less than that of the lung on the stimulated side and that the relative absorption of oxygen by the right and left lungs was unchanged.[5a] Determination of blood gas tensions in the experimental animal and in man and oximetry in the latter have confirmed the adequacy of ventilation by this method.[4a] The circulatory effects of this type of artificial respiration were of considerable interest, since it was found in the dog and in man that electrophrenic respiration had a more salutary effect on the circulation than positive pressure breathing after the circulation had been depressed by high spinal anesthesia [5b] or hemorrhagic shock.[6]

Perhaps the most significant observation in relation to bulbar poliomyelitis is the prompt and complete suppression of spontaneous respiration during electrophrenic respiration in the experimental animal and in

From the Department of Physiology, Harvard School of Public Health.
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1. Drinker, P., and Shaw, L. A.: An Apparatus for the Prolonged Administration of Artificial Respiration: I. A Design for Adults and Children, J. Clin. Investigation **7**: 229-247, 1929. Shaw, L. A., and Drinker, P.: An Apparatus for the Prolonged Administration of Artificial Respiration: II. A Design for Small Children and Infants with an Appliance for the Administration of Oxygen and Carbon Dioxide, ibid. **8**: 33-46, 1929.

2. Drs. Charles A. Janeway and R. Cannon Eley of the Children's Hospital and Dr. Louis Weinstein of the Haynes Memorial Hospital, Boston, and Dr. Albert G. Bower of the Los Angeles County General Hospital, Los Angeles, enabled us to study these cases during the 1949 epidemic of poliomyelitis.

3. From "Animal Magnetism" to Electrophrenic Respiration, editorial, New England J. Med. **242**: 340, 1950.

4. (*a*) Sarnoff, S. J.; Hardenbergh, E., and Whittenberger, J. L.: Electrophrenic Respiration, Am. J. Physiol. **155**: 1-9, 1948. Whittenberger, J. L.; Sarnoff, S. J., and Hardenbergh, E.: Electrophrenic Respiration: II. Its Use in Man, J. Clin. Investigation **28**: 124-128, 1949. (*b*) Sarnoff, S. J.; Whittenberger, J. L., and Hardenbergh, E.: Electrophrenic Respiration: III. The Mechanism of the Inhibition of Spontaneous Respiration, Am. J. Physiol. **155**: 203-207, 1948.

5. (*a*) Sarnoff, S. J.; Gaensler, E. A., and Maloney, J. V., Jr.: Electrophrenic Respiration: IV. The Effectiveness of Contralateral Ventilation During Activity of One Phrenic Nerve, J. Thoracic Surg. **19**: 929-941, 1950. (*b*) Sarnoff, S. J.; Maloney, J. V., Jr., and Whittenberger, J. L.: Electrophrenic Respiration: V. Effect on the Circulation of Electrophrenic Respiration and Positive Pressure Breathing During the Respiratory Paralysis of High Spinal Anesthesia, Ann. Surg., to be published. (*c*) Sarnoff, S. J.; Whittenberger, J. L., and Sarnoff, L. C.: Electrophrenic Respiration: VII. The Motor Point of the Phrenic Nerve, to be published.

6. Maloney, J. V., Jr.; Whittenberger, J. L.; Affeldt, J. E., and Sarnoff, S. J.: A Comparison of Effects of Positive Pressure Breathing and Electrophrenic Respiration on the Circulation During Hemorrhagic Shock and Barbiturate Poisoning, to be published.

man.[7] The cessation of central motor impulses to respiratory muscles, as observed grossly and by recording of action potentials,[7a] occurs within a few seconds after the onset of electrophrenic respiration. Since this prompt suppression of spontaneous respiration does not occur if the vagi are cut, it was concluded that the vagi provide a significant part of the afferent pathway for the inhibitory mechanism.[7] In normal, unanesthetized man, electrophrenic respiration by external stimulation causes prompt suppression of spontaneous respiration, an observation confirmed in over 400 instances. The patient, by a vigorous, voluntary effort, can breathe independently during electrophrenic respiration or can combat electrophrenic respiration by closing the glottis. This does not occur, however, unless such an effort is made. The data cited later herein support our early hope that in the patient with bulbar poliomyelitis all spontaneous respiration, including the respiratory irregularities, would be suppressed, thus permitting one to supply regular, effective respiration in these cases. At least one phrenic nerve must be partially or completely uninvolved in disease if this method is to be employed.

Since vagal stimulation during electrophrenic respiration would have been an undesirable concomitant of the method, bradycardia was carefully watched for in the first 100 human subjects on whom it was used. In no case was it observed.

METHOD

Arterial blood oxygen and carbon dioxide contents were determined by the method of Van Slyke and Neill.[8] Pneumotachograms, which made possible the subsequent determination of tidal and minute volumes, were obtained by the clinical unit devised by Silverman.[9] In all pneumotachograms inspiration is represented by a downward deflection (below the base line), the tidal volume being directly proportional to the area below the base line. Pneumograms were taken by means of an accordion rubber tubing placed around the upper part of the patient's abdomen; they were recorded simultaneously with the movements of the patient's right great toe on a two channel, direct-writing galvanometer via electromanometers.[10] Blood pressure was measured by auscultation.[11] In all instances but one, electrophrenic respiration was produced by application of a moistened, cloth-covered electrode, 4 mm. in diameter, externally over the skin at the site of the motor point of the phrenic nerve.[8c]

REPORT OF CASES

Data on 6 patients with respiratory dyskinesia are given.

CASE 1.—B. P., a boy 9 years of age, had been well until July 4, 1949, when he complained of a sore throat. This lasted three days and then subsided. On July 9 he was lethargic, and on July 11 he was nauseated and vomited once. The next day he had a stiff neck and a nasal quality in his voice. His temperature was 101 F. Lumbar puncture confirmed the diagnosis of poliomyelitis, and on July 13 he was brought to the Children's Hospital.

Physical examination revealed an acutely ill patient with labored and rapid but fairly regular respirations. The rectal temperature was 104 F. and the pulse rate 140. A puddle of mucoid material in the posterior pharynx could be voluntarily expelled by a definite effort, but the gag reflex was absent and the patient was unable to swallow. The voice had a definite nasal quality. The neck was stiff, and the patient was unable to flex it. Anterior neck muscle weakness was present. A questionable left facial nerve weakness was noted, and the left lower abdominal reflex was sluggish.

On July 14 the patient became less responsive and more restless. He vomited coffee ground material and passed three blackish brown stools. The Babinski signs became positive, and respirations became more labored and were less regular and coordinated than previously. The respiratory rate rose to 54. The pulse was variable in quality. Later that day it was decided that more adequate ventilation would benefit the patient, and the electrophrenic respirator was used. Prior to this, spontaneous respiration had become highly irregular (record of July 14, in fig. 1); stimulation of either phrenic nerve produced an effective, even ventilation with complete suppression of the irregular spontaneous respiration. The patient's extreme restlessness was completely alleviated during the use of the electrophrenic respirator and returned within two minutes after use of it was stopped. This observation was repeated numerous times. On the following morning (July 15) an electrode was surgically implanted on the right phrenic nerve. Adequate ventilation was accomplished by the phrenic respirator until 11 a. m., at which time the patient, still comatose, vomited large quantities of bile-stained fluid. During efforts to clear his airway, severe traction was made on the lead wire. A tracheotomy was performed. Soon afterward the right diaphragm ceased to respond. From then on respiration was maintained continuously by externally applied left phrenic stimulation for the ensuing three and a half days, with only brief interruptions to examine the adequacy of spontaneous breathing. In figure 1 can be seen the type and volume of spontaneous respiration (July 15, *A*), and also the effect of

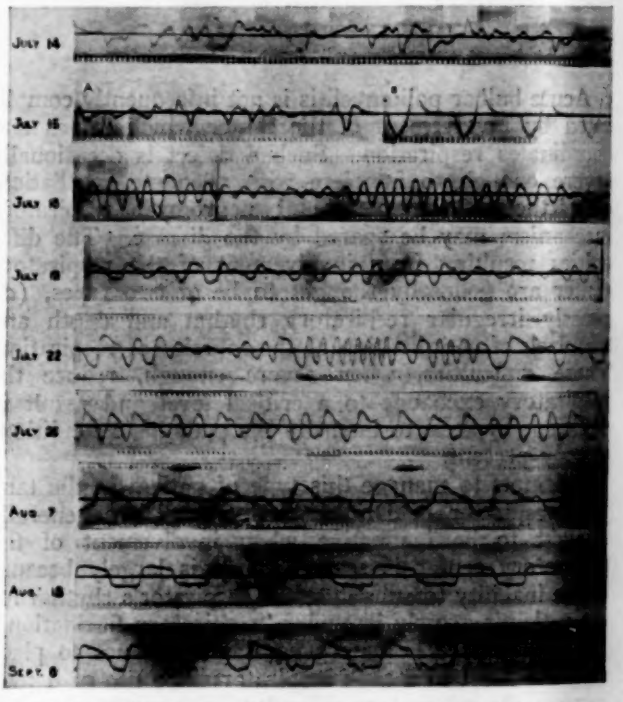

Fig. 1 (case 1).—Pneumotachograms on patient B.P.: July 14, spontaneous respiration showing gross irregularity; July 15, *A*, spontaneous respiration, and *B*, electrophrenic respiration; July 16, spontaneous respiration showing improvement in respiratory center to point where it is coordinating respiration although it is of Cheyne-Stokes type. Remaining pneumotachograms demonstrate gradual return to normal respiration. Inspiration is below the base line, expiration is above. The pneumotachograms of July 14, August 7 and September 6 were taken by face mask. The remainder were obtained by connection with the tracheotomy tube.

7. (*a*) Chatfield, P. O., and Sarnoff, S. J.: The Role of Pulmonary Proprioception in the Suppression of Spontaneous Breathing During Electrophrenic Respiration, to be published. (*b*) Sarnoff, Whittenberger and Hardenbergh.[6b]

8. Van Slyke, D. D., and Neill, J. M.: Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, J. Biol. Chem. **61**: 523-573, 1924.

9. Silverman, L.: Respiratory Air Flow Characteristics and Their Relation to Certain Lung Conditions Occurring in Industry, J. Indust. Hyg. & Toxicol. **28**: 183-196, 1946. Silverman, L., and Whittenberger, J. L.: Clinical Pneumotachograph, in Methods in Medical Research, Chicago, The Year Book Publishers, Inc., 1950, vol. 2, pp. 104-112; Instantaneous Air Flow Measurements, ibid., pp. 215-218.

10. Rappaport, M., and Sarnoff, S. J.: An Electronic, Multi-Range, Multi-Channel, Direct-Writing Pressure Recorder, Federation Proc. **8**: (pt. 1): 130, 1949.

11. Ragan, C., and Bordley, J., 3d: The Accuracy of Clinical Measurements of Arterial Blood Pressure, Bull. Johns Hopkins Hosp. **69**: 504-528, 1941.

electrophrenic respiration (July 15, *B*) in suppressing the irregular respiration and providing regular, effective respiration. During brief test periods off the respirator, respiration showed some improvement as far as coordination of intercostals and diaphragm was concerned, although it was still grossly irregular (fig. 1, July 16).

An attempt was made to record the consistently sedative effect of electrophrenic respiration on the restlessness of the patient. Simultaneous recordings of respiration and the movement of the right great toe are shown in figure 2. It can be seen that the patient was quiet during electrophrenic respiration and that restlessness became extreme when he was off electrophrenic respiration.

On July 18 it was noted that the left diaphragm was descending less vigorously in response to electrical stimulation, and at 8 a. m. the progressive crusting of the tracheotomy tube suddenly became severe and the patient became intensely cyanotic. Bronchoscopy was promptly performed, the tracheotomy tube replaced, and vigorous electrophrenic respiration maintained. This was followed by a prompt return to his previous state. In retrospect, this progressive block of the airways should have been noted earlier, since two of us had remarked that the drawing in of the intercostal spaces during diaphragmatic descent was gradually becoming more pronounced.

Later that day spontaneous respiration was again tried and found to be improved enough to justify trials without the phrenic respirator. At 4 a. m. on July 19, twelve hours after electrophrenic respiration had been stopped, it was noted that the patient's color was not optimal, that his respiration was

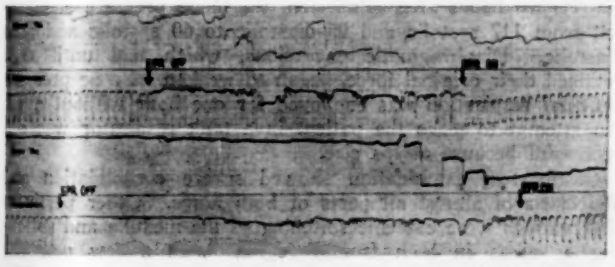

Fig. 2 (case 1).—The effect of electrophrenic respiration (EPR) on the restlessness which accompanied the respiratory irregularities of spontaneous respiration. Top two tracings are simultaneous and are taken while patient was breathing room air. Lower two tracings were taken after patient had been breathing 100 per cent oxygen for forty-five minutes. In each set of tracings the upper one indicates the patient's restlessness by recording the movements of the right great toe. Below that is the recording of respiration obtained with a simple pneumogram. Electrophrenic respiration was turned off at the first arrow and restarted at the second arrow in both records. See the accompanying table (page 1389) and comments.

more labored, that his blood pressure had risen to 180 systolic and 110 diastolic, and that the recently noted improvement in mental state had again reverted to deep coma. The electrophrenic respirator was applied, and this was followed by a prompt fall of the blood pressure to 120 systolic and 74 diastolic. Further hypertensive episodes of varying severity occurred while the patient was being weaned from the electrophrenic respirator. The hypertension responded to phrenic stimulation each time (fig. 3).

During this period it was apparent that the patient's central nervous system involvement was diminishing, as evidenced by his responsiveness and the improved character of his respiratory efforts. The respiratory center discharge (see fig. 1) had lost some of its chaotic character, and on July 21 it was considered wise to assist respiration by means of a chest respirator, because the left phrenic nerve was beginning to respond less and the skin over the phrenic motor point showed signs of irritation. Since the patient did not respond well to the chest respirator, he was transferred to a tank respirator for respiratory support as required for the ensuing five days.

During the period from July 19 to 21, when he was coming out of coma and reacting well to commands, it was the impression of the nurses in attendance that he could rest and sleep more readily and was less apprehensive while he was on electrophrenic respiration than while breathing spontaneously.

The patient had had several large tarry stools prior to electrophrenic respiration on July 14 and 15; he again began to pass numerous large tarry stools on July 21, and it was suspected that a Cushing type ulcer had developed. This probably accounted for the episodes of shock that were relieved only by vigorous replacement therapy. The details of this syndrome will be treated in a separate report.[12] Suffice it to say that gastrointestinal bleeding occurs more often in bulbar poliomyelitis than was previously supposed. Several weeks later, thorough roentgen examination of the gastrointestinal tract failed to reveal any abnormality.

It can be seen from the later tracings in figure 1 that the respiratory center gradually returned to normal, having gone from a condition of severe disorganization up through the Cheyne-Stokes type of breathing back to normal respiration. The patient's residual paralyses gradually disappeared almost completely. In December 1949 he could swallow, had gained weight almost to his presummer level and had recovered sufficiently to engage successfully in his favorite sports, ice skating and ice hockey. At that time fluoroscopy performed by his physician revealed "normal motion" of his left diaphragm and "fairly normal" motion on the right. On Feb. 1, 1950, fluoroscopy revealed "normal motion" of both diaphragms.

CASE 2.—E. J., a boy aged 17 years, was admitted Aug. 12, 1949, after four days of vomiting, headache, stiffness of neck, and fever (up to 104 F.). One day prior to admission, both

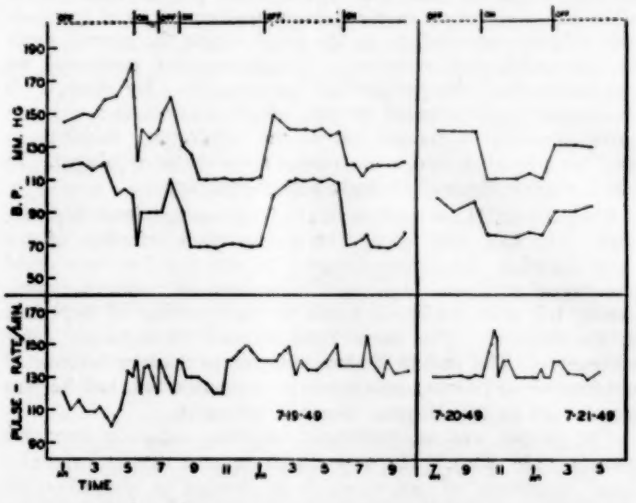

Fig. 3 (case 1).—Blood pressure and pulse rates during spontaneous and electrophrenic respiration during period when patient was being weaned from electrophrenic respiration.

his arms became weak and the patient noted difficulty in swallowing. Only four cells were found in the cerebrospinal fluid at that time. Just prior to admission, a second spinal tap revealed an increased number of cells. Physical examination revealed a well nourished boy in acute distress. The blood pressure was 140 systolic and 80 diastolic, the pulse rate was 110 per minute, the respiratory rate 28 per minute and regular. Rectal temperature was 102.8 F. The right facial nerve was paralyzed. The patient was unable to swallow, and the palate was deviated to the left. The neck was stiff to both flexion and rotation. Biceps, triceps, deltoid and other arm muscles were weak. The Kernig sign was positive. A diagnosis of bulbospinal poliomyelitis was made.

On Aug. 18, 1949 there was a sudden onset of irregular respiratory motions and the patient's color became poor. Oxygen was given by nasal catheter. Arterial pressure rose from 140 systolic and 90 diastolic to 200 systolic and 110 diastolic, and the pulse rate rose from 56 to 140 per minute. The only respiratory movements were spasmodic diaphragmatic twitchings. The patient was placed in a tank respirator operated at 25 cycles per minute, with intratank pressure operating from zero to minus 30 cm. of water. This forceful pressure gradient was used in an attempt to break through the patient's conflicting efforts and overbreathe him into apnea so that he would cease all spontaneous respiratory effort. The patient

12. Hartmann, J. R.; Cook, C. D.; Sarnoff, S. J., and Berenberg, W.: Gastro-Intestinal Lesions in Bulbar Poliomyelitis, to be published.

was almost comatose at this time. Over a period of thirty minutes it was noted that the patient resisted the respirator violently and that his ventilatory exchange was inadequate. In view of his worsening condition, he was removed from the tank respirator and artificial respiration was started by the Schaefer prone pressure method, but respirations were still irregular and incoordinated about twenty minutes later when electrophrenic respiration was started. The right phrenic nerve was almost wholly unresponsive, but a vigorous diaphragmatic response was obtained on the left and all spontaneous respiratory irregularities ceased within a few seconds after electrophrenic respiration was applied. The patient was breathing with electrophrenic respiration for eight hours (fig. 4), after which it was found that spontaneous respiration had become more regular and apparently was adequate. It appeared that the temporary respiratory help was sufficient to tide the patient over a critical period. The arterial pressure returned to normal limits soon after the beginning of electrophrenic respiration.

On Aug. 22, 1949 the patient's respirations again became grossly irregular and shallow, he became cyanotic, the pulse rose to 130, and the arterial pressure rose to 210 systolic and 100 diastolic. Electrophrenic respiration was attempted, but on neither side did the diaphragm respond appreciably, and the patient was placed in a tank respirator. The efforts at resisting the tank respirator were feeble, presumably because of extensive additional respiratory motor neuron involvement, and the tank was able to overventilate to the point where the central drive to respiration was removed. Roentgenograms confirmed an impression that the patient had pneumonitis. By August 30 the patient had recovered enough left diaphragmatic and intercostal function to remain out of the respirator. Inability to swallow persisted, and a gastrostomy had to be employed. In other respects the patient made a good recovery.

Case 3.—D. H., a white man aged 29, was admitted Sept. 10, 1949. He had mild upper respiratory tract infection of ten days' duration. In another hospital, he was noted to have slight pharyngeal paralysis, high right diaphragm on roentgen examination, left arm weakness, headache, and pooling of secretions in the pharynx. The spinal fluid showed 131 cells per cubic millimeter. The patient became difficult to manage because of pharyngeal secretions; poliomyelitis was suspected, and he was transferred to the Haynes Memorial Hospital.

The patient was an extremely tall man weighing over 300 pounds (136 Kg.). He was comatose and deeply cyanotic; large quantities of secretions were pooled in the pharynx. Generalized muscular twitchings were observed. Arterial blood pressure was 195 systolic and 120 diastolic. Respirations were irregular in depth and rhythm, with a rate of 14 per minute.

The patient was given oxygen by nasal catheter, and the airway was aspirated almost continually for two hours to

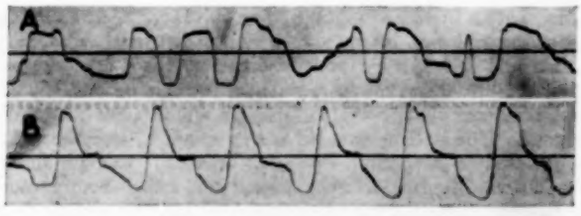

Fig. 4 (case 2).—Pneumotachograms on patient E.J.: *A*, spontaneous respiration; *B*, electrophrenic respiration. Inspiration is below the base line, expiration is above.

remove large quantities of secretions. He vomited several times, and it was thought likely that he had previously aspirated quantities of vomitus into his lungs. It was impossible to maintain an adequate airway by nasopharyngeal suction; because the patient was occasionally deeply cyanotic, a tracheotomy was performed. After this, each inspiratory effort brought air to the lungs, as indicated by auscultation. Nevertheless, respirations remained shallow and irregular. Since the airway was free, it was believed that respiratory center dysfunction must be the source of the patient's difficulty.

Electrophrenic respiration was started on the left with an external electrode. Spontaneous respiration and irregularities were promptly suppressed, and the patient's color soon returned to normal and remained so. Within fifteen minutes the patient was out of coma and responded to stimuli. The muscular twitching had disappeared. Test of right diaphragmatic activity was made by stimulation of the right phrenic nerve, with excellent response. Within two hours the blood pressure fell from 195 systolic and 120 diastolic to 120 systolic and 85 diastolic. Twelve hours after admission, while still receiving

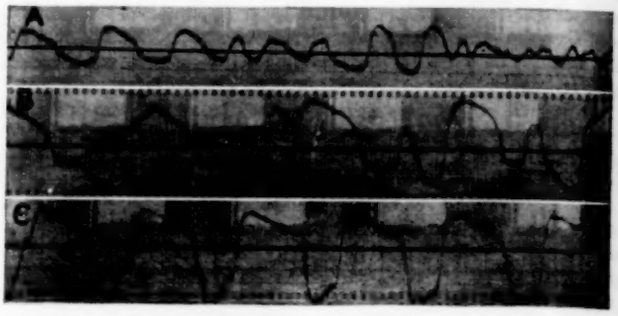

Fig. 5 (case 4).—Pneumotachograms on patient W.W.: *A*, spontaneous respiration; *B*, tank respiration, and *C*, electrophrenic respiration. Inspiration is below the base line, expiration is above. Taken through connection with tracheotomy tube.

electrophrenic stimulation, the patient was attempting to talk and answered questions correctly by nodding his head. However, from the time of his admission until death, thirty-two hours later, the body temperature rose steadily from 101 to 107 F. Thirty-two hours after admission, the blood pressure suddenly fell from 117 systolic and 95 diastolic to 60 systolic and zero diastolic. Diaphragmatic excursions, which had until then retained their original force, began to weaken. Prone pressure artificial respiration was employed for one hour without avail. An attempt to place the patient in a tank respirator was not successful because of his size.

Postmortem examination showed severe consolidation and atelectasis of almost all parts of both lungs. Other pertinent observations were extreme softening of the medulla and softening of areas in both frontal regions with a few petechial hemorrhages.

Case 4.—W. W., a white man aged 24, was admitted to Los Angeles County General Hospital Aug. 8, 1949. The diagnosis was bulbar poliomyelitis. A tracheotomy was done on admission. On the second day after admission, the temperature rose to 105 F. and respiratory irregularities were noted (fig. 5 *A*). The patient appeared to be using his diaphragm little, if at all, and was accomplishing most of his ventilation with intercostal muscles. He was placed in the tank respirator, but, although this appeared to accomplish adequate ventilation, spontaneous irregularities were not suppressed and the patient continued to resist the respirator (fig. 5 *B*).

Electrophrenic respiration was applied at this time, and it completely suppressed spontaneous respiration and irregularities (fig. 5 *C*). With the change of the pressure gradient from 15 to 25 cm. of water, the tank respirator was later able to suppress spontaneous respiration. This suppression occurred only after an interval long enough to lead one to suspect that it resulted from hyperventilation rather than reflex inhibition of the respiratory center.

Case 5.—C. R., a white girl aged 6 years, was admitted to the Los Angeles County General Hospital Aug. 6, 1949. The diagnosis was bulbospinal poliomyelitis. A tracheotomy was done on August 7. On the third hospital day the patient was placed in an adult-type respirator because of respiratory irregularities and apparent weakening of diaphragmatic and intercostal movements. The patient's own respiratory rate was 32 per minute, spasmodic and irregular in nature. At this time the patient was removed from the respirator (maximum rate of which is about 25 per minute) and electrophrenic respiration was tried, first on one side, then the other. In both instances it immediately suppressed the irregular spontaneous respiration. The following note was made by the resident:

"The patient had been breathing erratically since being put into a (tank) respirator approximately eighteen hours prior

to electrophrenic respiration. She definitely did not coordinate. She had improved somewhat and coordination was more nearly achieved, but it was nevertheless thought wise to transfer the patient to a junior-sized respirator. During the transfer she was allowed to breathe independently. Spontaneous respiration was noted to be irregular both in rate and depth. Electrophrenic respiration was applied with striking results. Respirations immediately became regular and deep and remained so throughout the twenty minutes of phrenic respiration. Her color, which was borderline while she was breathing spontaneously, improved with electrophrenic respiration. Ventilation appeared to be completely adequate. After electrophrenic respiration, while the patient was breathing unassisted, ventilation did not appear to be adequate and her color again became borderline."

After this patient was transferred to a junior-sized respirator, the maximal rate of which was 44 per minute, like W. W. (case 4), she coordinated with the respirator, not immediately but after an interval in which it might be supposed that enough hyperventilation had occurred to remove the chemical respiratory drive.

CASE 6.—M. H., a pregnant woman, was admitted to the Haynes Memorial Hospital on Oct. 14, 1949 with a diagnosis of acute paralytic poliomyelitis. One week before admission she had a mild "pleurisy," but she felt well until two days prior to admission, at which time she noted headache, nausea, vomiting, stiff neck and a temperature of 100 F. The patient was in the sixth month of a normal pregnancy. Cerebrospinal fluid findings were consistent with the diagnosis of poliomyelitis. Paralytic involvement included both triceps and, to some extent, the shoulder girdles.

On October 16 the patient became lethargic and her respiration labored. She became cyanotic and was difficult to arouse. Respirations were grossly irregular with obvious paradox involving the diaphragm and intercostal muscles. Extrasystoles, which had been previously noted, now became much more numerous. Electrophrenic respiration was started on the right, and effective diaphragmatic contractions resulted in suppression of the respiratory irregularities, prompt improvement of the patient's color and disappearance of the extrasystoles. The presence of extrasystoles during spontaneous respiration and their absence during electrophrenic respiration was confirmed several times. Her blood pressure fell from 150 systolic and 90 diastolic during spontaneous respiration to 120 systolic and 75 diastolic during electrophrenic respiration. After one hour of electrophrenic respiration the patient's spontaneous respiration had largely lost its irregular quality; she was placed in a tank respirator, which promptly took control of respiration. The previously noted extrasystoles were absent while the patient was in the tank respirator. Subsequent progress of the disease confined the patient to the tank respirator, except for brief periods, until after the delivery of a normal 6 pound (2,722 Gm.) son on Jan. 8, 1950. Since then she has rapidly improved, being free of the respirator since March 7, 1950.

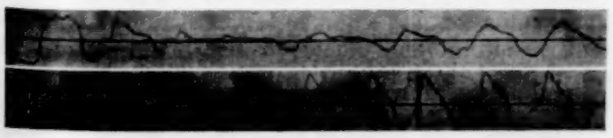

Fig. 6 (case 7).—Pneumotachograms on patient G.W.: *A*, spontaneous respiration; *B*, electrophrenic respiration. Inspiration is below the base line, expiration is above.

Data from 2 additional cases are reported briefly, inasmuch as they were cases of bulbar poliomyelitis with respiratory center involvement that produced gross irregularity of spontaneous respiration. Ventilation, when observed by the authors, was thought to be adequate in these patients in spite of the irregular type of respiration, and respirator treatment was not thought to be required. They are presented as additional cases in which it was demonstrated that the grossly irregular respiration of bulbar poliomyelitis can be suppressed with electrophrenic respiration.

CASE 7.—G. W., a boy 9½ years of age, was admitted July 28, 1949 on the sixth day of his illness; the diagnosis of bulbar poliomyelitis was made on admission and confirmed by spinal fluid observations. The moderately irregular type of spontaneous respiration in this patient is shown in figure 6 *A*. Within a few seconds after the application of left-sided electrophrenic stimulation, the irregularities disappeared and were supplanted by a regular and effective ventilatory effort (fig. 6 *B*).

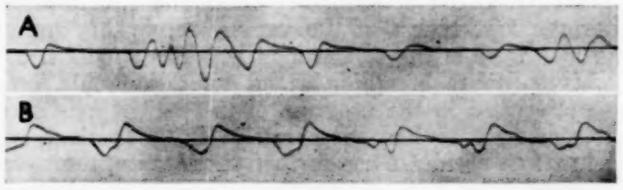

Fig. 7 (case 8).—Pneumotachograms on patient R.H.: *A*, spontaneous respiration; *B*, electrophrenic respiration. Inspiration is below the base line, expiration is above.

CASE 8.—R. H., a boy 9½ years of age, entered the hospital on Sept. 2, 1949, with a diagnosis of bulbar poliomyelitis. A spinal tap revealed 240 white cells, all lymphocytes. Total protein was 52.2 mg. per hundred cubic centimeters. He was tested with the electrophrenic respirator on Sept. 7, 1949. Figure 7 *A* shows the patient's grossly irregular spontaneous respiration, which was promptly suppressed by electrophrenic respiration as shown in figure 7 *B*. The last three breaths in the lower tracing are included to demonstrate how particles of mucus can interfere with ventilation even though the respiratory effort is uniform and may appear uniformly effective to visual observation. This observation underscores the necessity for maintaining a perfectly free airway.

COMMENT

The general opinion concerning the use of the tank respirator in the treatment of central respiratory involvement in poliomyelitis is that its use is only infrequently of demonstrable aid.[13] The report of Galloway and Seifert[14] tends to suggest that more profitable use of the tank respirator may be made. However, it is well known that bulbar poliomyelitis may show widely varying degrees and intensity of respiratory involvement.

Are Respiratory Irregularities Due Solely to Airway Disturbance?—In reference to the studies of Galloway and Seifert,[13] these authors performed a distinct service in highlighting the necessity for keeping the airway clear. Likewise there can be little doubt that, on superficial examination of a patient with irregular respiration, there may be difficulty in deciding whether or not the central respiratory drive is functioning properly. However, the implication of Galloway and Seifert[13] is that the latter condition either does not exist or is of only incidental importance. This point of view does not appear to be compatible with the evidence presented herein. Patients subjected to tracheotomy, in whom freedom from airway obstruction was confirmed by pneumotachograms and blood gas tension data, still exhibited grossly irregular respiration which can be understood only by postulating involvement of the respiratory center.

Severity of Respiratory Center Disorganization from Which Recovery May Occur.—On July 16, 1949 (fig. 1), patient B. P. (case 1) exhibited Cheyne-

13. Wilson, J. L.: Outline of Essential Treatment of Bulbar Poliomyelitis, J. South Carolina M. A. **44**: 354-357, 1948; Outline of Essential Treatment of Bulbar Poliomyelitis, The First International Poliomyelitis Conference, Philadelphia, J. B. Lippincott Company, 1949, p. 248; The Use of the Respirator in Poliomyelitis, New York, National Foundation for Infantile Paralysis, publication No. 23, revised July, 1947. Edwards, W. M.: Analysis of Fatal Cases of Poliomyelitis, California Med. **69**: 367-374, 1948.

14. Galloway, T. C., and Seifert, M. H.: Bulbar Poliomyelitis, J. A. M. A. **141**: 1-6 (Sept. 3) 1949.

Stokes breathing. Almost invariably the appearance of Cheyne-Stokes breathing has been considered an indication of the worsening of a patient's clinical state. The contrary was true in this patient, as shown by the pneumotachograms from the two preceding days (July 14 and 15, fig. 1). In comparison, the Cheyne-Stokes breathing represented a relatively high degree of respiratory center organization, since it indicated at least some degree of effective ventilatory effort and also indicated for the first time that the various respiratory muscle groups were acting synchronously. The appearance of Cheyne-Stokes breathing as an indication of a great step forward in the progress of the patient may serve to demonstrate how desperately ill the patient was when first seen. It has further significance, moreover, in confirming the opinion that the essential difficulty in this tracheotomized patient was due to involvement of the respiratory center and not to an inadequate airway.

These studies provide physiologic confirmation of the anatomic observation of Baker[15] and his associates in which verified medullary lesions were correlated with the occurrence of respiratory irregularities in patients with bulbar poliomyelitis.

There can be no doubt that maintaining an adequate airway and avoiding the harmful effects of hypoxia and high carbon dioxide levels in the blood by whatever means remains a basic principle in the treatment of bulbar poliomyelitis. It is of prime importance, however, to remember that respiratory center involvement contributes significantly to the respiratory dyskinesias and inadequate ventilation seen in this disease and must be countered with some form of artificial respiration as soon as the respiratory defect becomes significant.

Usefulness of the Tank Respirator in Management of Respiratory Irregularities of Bulbar Poliomyelitis.—Although past experience suggested that in patients with bulbar poliomyelitis in whom an adequate airway had been provided the tank respirator did not suppress the patient's irregular spontaneous respiratory efforts, recent experience elsewhere and our experiences with patients C. R. (case 5) and W. W. (case 4) suggest that, by utilizing larger pressure gradients than those commonly employed and consequently producing hyperventilation and alkalosis, the tank respirator may be more effective. It is not certain from present data whether the electrophrenic respirator, like the tank respirator, will be incapable of suppressing spontaneous respiration without significant hyperventilation in patients with bulbar poliomyelitis. Consideration[7a] of the neurogenic mechanism whereby electrophrenic stimulation inhibits the respiratory center makes it likely that hyperventilation will not be required. Further, since the tank respirator (using negative intratank pressure) is physiologically the same as positive pressure breathing,[16] the use of high pressure gradients with the tank respirator may be limited by the known deleterious effect of positive pressure breathing in patients whose cardiac output is already at critically low levels, due to either peripheral vasomotor collapse or diminished blood volume.[17]

It was believed by those who observed patient B. P. (case 1) that the tank respirator would have exerted little influence on his respiratory irregularities during the acute stage of his disease. Although it would have been desirable from an experimental point of view to have compared the effects of the tank respirator and the electrophrenic respirator in this patient, the primary consideration was to maintain the patient in an optimal respiratory status while he was so desperately ill. After the period of critical illness, a comparison would have been irrelevant. A tank respirator was not used on patient D. H. (case 3) not only because of the respiratory arrhythmia and incoordination but because of his massive size. A later attempt showed that it was physically impossible to place him in a respirator.

In patients whose respiratory irregularities were moderate and who eventually yielded to larger pressure gradients in the tank respirator, the period of time required to obtain cessation of spontaneous respiration suggested that overventilation was the mechanism rather than reflex suppression as seen with electrophrenic respiration.[7] If this premise is correct, it makes implicit the assumption that control of respiration with the tank respirator can be achieved only by producing alkalosis. While the data from patient B. P. (case 1) do not demonstrate that long term control with electrophrenic respiration can be achieved without hyperventilation, this patient's alkalosis was probably due to overestimation of ventilatory requirements rather than inability to control respiration without overbreathing. Finally, the most conclusive demonstration is given by the data on patient E. J. (case 2). This patient was placed in a tank respirator during his first respiratory crisis, and it was noted that even the use of vigorous pressure gradients (negative pressure of 30 cm. of water) failed to help him or to influence his respiratory irregularities. In contrast, the use of electrophrenic respiration promptly suppressed his respiratory irregularities and sustained him over the initial period of crisis.

How Much Ventilation?—As with all methods of artificial respiration, the problem of determining optimal ventilation in a given situation is complicated. There is reason to believe, however, that ventilation appropriate to the needs of the body can be more accurately achieved by electrophrenic respiration than by other methods. First, in normal subjects electrophrenic respiration inhibits spontaneous breathing only when adequate ventilation is supplied; this level of ventilation can be bracketed by adjustment of the controls between slight hypoventilation and slight hyperventilation; second, the tank respirator and other pressure breathing methods are resisted by the proprioceptive pulmonary reflexes; in normal persons the result of the conflict is hyperventilation. The effect of the reflexes can be abolished only by significant hyperventilation. The extent to which these observations hold in bulbar poliomyelitis has not been defined.

Observations of the patient's color can be notoriously misleading,[18] and even when the arterial oxygen saturation is known to be normal there is no assurance that excretion of carbon dioxide is adequate, especially if the patient is receiving oxygen at the time. This fact has been known to investigators interested in resuscitation[19] but is not generally appreciated by the clinician.

15. Baker, A. B.: Neurologic Signs of Bulbar Poliomyelitis, The First International Poliomyelitis Conference, Philadelphia, J. B. Lippincott Company, 1949, p. 241.

16. Maloney, J. V., Jr., and Whittenberger, J. L.: Circulatory Effects of Pressure Breathing in the Body Respirator, Am. J. Med. **8**: 393, 1950.

17. Beecher, H. K.; Bennett, H. S., and Bassett, D. L.: Circulatory Effects of Increased Pressure in the Airway, Anesthesiology **4**: 612-618, 1943. Eather, K. F.; Peterson, L. H., and Dripps, R. D.: Studies of the Circulation of Anesthetized Patients by a New Method of Recording Arterial Pressure and Pressure Pulse Contours, ibid. **10**:125-132, 1949. Sarnoff, Maloney and Whittenberger.[6b] Maloney, Whittenberger, Affeldt and Sarnoff.[9]

18. Comroe, J. H., Jr., and Botelho, S.: Unreliability of Cyanosis in Recognition of Arterial Anoxemia, Am. J. M. Sc. **214**: 1-6, 1947.

19. Whitehead, R. W.; Spencer, J. N.; Parry, J. M., and Draper, W. B.: Studies on Diffusion Respiration: IV. The Oxygen and Carbon Dioxide Content and the Hydrogen Ion Concentration of Arterial and Venous Abdominal Blood of Dogs During Diffusion Respiration, Anesthesiology **10**: 54-60, 1949.

Simple determinations of respiratory minute volumes indicate whether respiration is in approximately the proper range for the person. A variety of devices are available for that purpose; however, such measurements lose their predictive value in the presence of faulty air distribution and/or increased diffusion barriers in the lung, which unfortunately often occur in bulbar poliomyelitis. Analysis of arterial blood gas content and partial pressures, although cumbersome, might well be used more widely in those centers that are equipped for this purpose. What is needed is some form of analyzer, either of blood p_H or pCO_2 (carbon dioxide concentration expressed in terms of pressure) or alveolar carbon dioxide, which will feed back into and regulate the depth of respiration. Such a device would provide the electrophrenic respirator with some of the coordinative properties of the respiratory center.[20]

It cannot be stated at the present time that electrophrenic respiration has an unequivocal area of usefulness in the treatment of bulbar poliomyelitis. It seems, however, that should the method prove generally feasible in the hands of clinicians, it might be of help because of the following considerations:

A. *Suppression of Spontaneous Respiration Including Respiratory Incoordination.*—This was discussed previously. In every instance of respiratory irregularity due to bulbar poliomyelitis which we have seen and in which one phrenic nerve has yielded an adequate response, those irregularities have been suppressed and regular respiration has been provided.

B. *Effect on Blood Pressure.*—1. Hypertension: Detailed studies are not available except on patient B. P. (case 1), in whom hypertension was promptly relieved after the application of electrophrenic respiration (fig. 3). Whether this was due to relief of anoxia or to some as yet undefined neurogenic mechanism cannot be stated. Three other patients with hypertension showed a similar response to electrophrenic respiration (cases E. J., D. H. and M. H., cases 2, 3 and 6).

2. Shock: In previous experiments in both man and dog it has been demonstrated that when the organism is in shock due to either blood loss or sympathetic blockade (high spinal anesthesia), positive pressure breathing significantly decreases venous return, cardiac output and blood pressure.[21] Comparisons between electrophrenic respiration and positive pressure breathing in these circumstances revealed that negative intrapleural pressure breathing (electrophrenic respiration), by encouraging venous return, consistently maintained a higher blood pressure and cardiac output.[21] Since artificial respiration with negative intratank pressure in the respirator is (in terms of the effect on the circulation) the same as positive pressure breathing,[16] electrophrenic respiration is likely to be of advantage to the circulation when shock is present.

C. *Sedative Effect on Restless Patients.*—The strikingly consistent response of patient B. P. (case 1) indicated that electrophrenic respiration was bringing about some change that removed the stimulus to restlessness. It cannot be decided at present whether changes in the blood gas levels or neurogenic mechanisms induced the quiet state, but the motion pictures taken at the time [22] as well as the numerous observers who saw this patient confirmed the changes recorded in figure 6. The same effect was noted in a less precise way in all but one of the other patients studied. When the data from the accompanying table are correlated with figure 2, there is little to support the assumption that arterial hypoxia was responsible for the restlessness exhibited during the brief periods of spontaneous respiration that were permitted in the first days of treatment. The levels of serum carbon dioxide were likewise not suggestive of a relationship between restlessness and respiratory acidosis. Many more data are needed.

D. *Nursing Care.*—There are few diseases in which the nursing care and attention to detail are of more decisive importance to the patient's outcome than in bulbar poliomyelitis. There is a great difference in the difficulties encountered in caring for a bed patient and one enclosed in a respirator. One clinical determination alone, that of taking the blood pressure, not only would be facilitated but would be more accurate by virtue of being freed from the fluctuating intratank reference base line. Other advantages are obvious.

E. *Acclimatizing the Patient with Bulbar Poliomyelitis to the Tank Respirator.*—It is not unlikely that the tank respirator, although it may not be able to achieve control of respiration, may be able to maintain control of respiration once it has been established. It has been suggested that one eventual application of electrophrenic respiration may be to adapt the refractory patient to the tank respirator should it become desirable to do so. The experience with patient M. H. (case 6) supports this hope.

*Arterial Oxygen Saturation and Carbon Dioxide Content of Serum of B. P. (Case 1) During Electrophrenic Respiration and Brief Periods of Spontaneous Breathing**

No. Sample	Time	% Arterial O_2 Saturation	Vols. % Serum CO_2 Content	Remarks
	Breathing Room Air			
1	48 min. before EPR turned off	101	27.3	On EPR; not restless
2	80 min. after EPR turned off	94	35.3	Spontaneous irregular respiration; restless
3	132 min. after EPR restarted	100	31.7	On EPR; not restless
	Breathing 100% Oxygen (into Tracheotomy tube)			
1	34 min. before EPR turned off	111	29.6	On EPR; not restless
2	110 min. after EPR turned off	112	31.3	Spontaneous irregular respiration; restless
3	274 min. after EPR turned off	112	31.6	Spontaneous irregular respiration; restless
4	108 min. after EPR restarted	112	30.5	On EPR; not restless

* The letters EPR denote electrophrenic respiration.

SUMMARY AND CONCLUSIONS

1. Respiratory center involvement in bulbar poliomyelitis contributes significantly to the respiratory arrhythmia and dyskinesia seen in that disease.

2. In 9 patients with central respiratory irregularities due to bulbar poliomyelitis, the irregularities could be suppressed in each case by electrophrenic respiration and regular effective ventilation provided instead.

3. More forceful pressure gradients may enlarge the area of usefulness of the tank respirator in bulbar poliomyelitis, but it is to be emphasized that negative intratank pressure breathing is essentially the same as positive pressure breathing by face mask or endotracheal tube, including the effects on the circulation. Therefore, if higher pressure gradients are used, even more circumspect analysis of the patient's circulatory status should be made. Patients with low blood volume and/or low blood pressure and/or an inadequate cardiac output tolerate positive pressure breathing poorly and in direct proportion to the circulatory deficiency. The electrophrenic respirator is not a hazard in the presence of circulatory inadequacy and may actually elevate the blood pressure and cardiac output in these circumstances.

4. The usefulness of the electrophrenic respirator cannot be considered as established in bulbar poliomyelitis until additional experience has been obtained, but the foregoing data are encouraging. The apparatus should not be used unless the operator has acquired sufficient proficiency in its use. However, practice on normal volunteers is readily acquired. It is obvious

20. Kuehue, P., and Kolmar, D.: Die Regulation der Ventilationsgroesse der eisernen Lunge mit Hilfe des CO_2-Gehaltes der Ausatmungsluft, Deutsche Gesundheitswes. **5**: 35-39, 1950.

21. Maloney, Whittenberger, Affeldt and Sarnoff.[6] Sarnoff, Maloney and Whittenberger.[5b]

22. Dr. William Berenberg pointed out the value of motion picture studies of this patient.

that one phrenic nerve must be wholly or partially uninvolved by disease if effective electrophrenic respiration is to be performed.

5. The extraordinary extent and severity of central nervous system derangement that can exist and still be reversible if the critical demands of the respiratory and circulatory systems are met have been demonstrated.

6. The electrophrenic respirator consistently and strikingly diminished the restlessness and hypertension in 1 patient and achieved similar results in others. The mechanisms involved are not known.

7. It was thought that nursing care was facilitated in the treated group of patients in comparison to what is usually the case with tank-enclosed patients.

MYELOID METAPLASIA

MATTHEW BLOCK, M.D.
and
LEON O. JACOBSON, M.D.
Chicago

Myeloid metaplasia is a clinical and pathologic syndrome of varied cause which is characterized by the constant occurrence of extramedullary hematopoiesis in the spleen and almost always in the liver, splenomegaly and usually hepatomegaly, and an anemia with immature red and white cells in the peripheral blood. Because of its resemblance to leukemia it has been frequently diagnosed as such,[1] and even today there is a difference of opinion concerning its relation to leukemia.[2] As a result of this confusion it has been described under at least twenty-five different names.[3] Many of the cases of myeloid metaplasia reported in the literature were diagnosed only at autopsy or at splenectomy [4]; in others, a diagnosis of sclerosis of the marrow was made but the presence of myeloid metaplasia of the liver and spleen was not proved,[5] which is significant because myelosclerosis may exist without myeloid metaplasia.[6]

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1. (*a*) Thompson, W. P., and Illyne, C. A.: Clinical and Hematologic Picture Resulting from Bone Marrow Replacement, M. Clin. North America **24**: 841-853, 1940. (*b*) Anagnostu, J. L.: Beitrag zum Studium der systematischen Osteosklerosen, Folia haemat. **50**: 70-84, 1933. (*c*) Mettier, S. R., and Rusk, G. Y.: Fibrosis of the Bone Marrow (Myelofibrosis) Associated with a Leukemoid Blood Picture: Report of 2 Cases, Am. J. Path. **13**: 377-388, 1937. (*d*) Custer, R. P., and Crocker, W. J.: The Myeloleukaemoid Blood Picture Associated with Tuberculosis, Folia haemat. **46**: 359-366, 1932.

2. (*a*) Arneth: Myeloisch-pseudoleukämische Reaktion ("aleukämische Myelose") und Milzexstirpation bei qualitativer Betrachtung, Wien. med. Wchnschr. **82**: 1544-1546, 1932. (*b*) Engelbreth-Holm, J.: Spontaneous and Experimental Leukaemia in Animals, London, Oliver & Boyd, Ltd., 1942. (*c*) Heller, E. L.: Aleukemic Myelosis: Chronic Non-Leukemic Myelosis, Agnogenic Myeloid Metaplasia, Osteosclerosis, Leuko-Erythroblastic Anemia, and Synonymous Designations, Am. J. Path. **23**: 327-365, 1947. (*d*) Hugonot, G., and Sohier, R.: Splénomégalie myéloïde mégacaryocytaire amyélocythémique et tuberculose, Sang **9**: 933-952, 1935. (*e*) Mettier, S. R., and Purviance, K.: Leukemia Without Leukocytosis (Aleukemic Myelosis) and Without Splenomegaly, Arch. Int. Med. **60**: 458-473 (Sept.) 1937. (*f*) Jackson, H., Jr.; Parker, F., Jr., and Lemon, H. M.: Agnogenic Myeloid Metaplasia of the Spleen: A Syndrome Simulating Other More Definite Hematologic Disorders, New England J. Med. **222**: 985-994, 1940. (*g*) Jordan, H. E., and Scott, J. K.: Case of Osteosclerosis with Extensive Extramedullary Hemopoiesis and Leukemic Blood Reaction. Arch. Path. **32**: 895-909 (Dec.) 1941. (*h*) Weil, P. E.; Isch-Wall, P., and Perlès, S.: La ponction de la rate: Procédé de diagnostic cytologique, Paris, Masson & Cie, 1936.

3. (*a*) Hirschfeld, H.: Die generalisierte aleukämische Myelose und ihre Stellung in System der leukämischen Erkrankungen, Ztschr. f. klin. Med. **80**: 126-173, 1914. (*b*) Hickling, R. H.: Chronic Non-Leukemic Myelosis, Quart. J. Med. **30**: 253-275, 1947. (*c*) Paolino, W.: The Syndrome of Pseudo-Leukemic (Pseudo-Erythemic) Myelosis, Acta haemat. **2**: 86-109, 1949. (*d*) Heller.[3c]

4. (*a*) Reich, C., and Rumsey, W., Jr.: Agnogenic Myeloid Metaplasia of Spleen: Report of 5 Cases Illustrating Diagnostic Difficulties and Danger of Splenectomy and Radiation Therapy, J. A. M. A. **118**: 1200-1204 (April 4) 1942. (*b*) Thompson and Illyne.[1a] Mettier and Rusk.[1c] Arneth.[2a]

5. Rosenthal, N., and Erf, L. A.: Clinical Observations on Osteopetrosis and Myelofibrosis, Arch. Int. Med. **71**: 793-813 (June) 1943.

6. Engell, H. C.: Myelosclerosis, Acta med. Scandinav. **129**: 371-380, 1947.

It is therefore our purpose in this paper to attempt to clarify the position of myeloid metaplasia relative to leukemia and to describe the clinical characteristics of this syndrome and the methods of making an antemortem diagnosis. It is furthermore our intent to show that the cases reported under various names such as nonleukemic myelosis,[3b] aleukemic myelosis [2a, c] and erythroleukemia [7] and various combinations of names reflecting the cell type or organ most extensively involved or the alleged degree of resemblance to leukemia are all essentially the same syndrome.

COMPARATIVE ANATOMY OF HEMATOPOIESIS

The comparative anatomy of hematopoiesis has been reviewed by Jordan [8] and Maximow.[9] According to their descriptions hematopoiesis occurs in the cyclostomes as diffuse areas of erythroid or lymphogranulopoietic cells in the wall of the gut and in the loose connective tissues in general. Important sites of hematopoiesis in the fish and urodeles are the spleen, liver, intestinal tract, gonads and mesonephron with the spleen being primarily erythropoietic and the other organs producing lymphocytes and granulocytes. In the Anura hollow bones containing hematopoietic marrow appear for the first time, and there is a seasonal variation in the activity of this marrow so that at the time that the marrow is inactive the spleen assumes its function,[8] much as occurs in patients with myeloid metaplasia. In still higher adult vertebrates in general and in mammals in particular, myeloid tissue is concentrated almost exclusively in the marrow under normal conditions, although under abnormal conditions and in the normal embryo a condition reminiscent of that in lower vertebrates is encountered.

EMBRYONIC DEVELOPMENT OF HEMATOPOIESIS IN MAMMALS

The occurrence of nonleukemic extramedullary hematopoiesis (myeloid metaplasia) in mammals has a firm basis in embryology. During early developmental stages in the mammalian embryo hematopoiesis is a function of the connective tissues as a whole.[10] Embryonic connective tissue in every location in the embryo, including the central and peripheral nervous system, is capable of giving rise to cells which are formed normally to a significant extent only in the bone marrow of the adult.[11] Under experimental conditions it is possible to cause embryonic organs and tissue which have lost the ability to produce myeloid cells or normally only manifest this ability in slight degree to produce these cells in large numbers.[12]

EXPERIMENTAL PRODUCTION OF MYELOID METAPLASIA IN POSTNATAL LIFE IN MAMMALS

It is probable that in many sites of the adult mammal mesenchymal cells remain which, under certain stimuli, are capable of assuming their embryonic potentialities.[13]

7. diGuglielmo, S.: L'érythrémie aïgue, Rev. belg. sc. méd. **10**: 200-215, 1938.

8. Jordan, H. E.: Extramedullary Blood Production, Physiol. Rev. **22**: 375-384, 1942.

9. Maximow, A.: Bindegewebe und Blutbildende Gewebe, in Handbuch der Mikroskopischen Anatomie des Menchen, edited by Wilhelm von Möllendorff, Berlin, Julius Springer, 1927, vol. 2, pt. 1.

10. Maximow, A.: Untersuchungen über Blut und Bindegewebe: I. Die frühesten Entwicklungstadien der Blut und Bindegewezellen beim Säugetier-Embryo, bis zum Anfang der Blutbildung in der Leber, Arch. f. mikr. Anat. **73**: 444-561, 1909. Bloom, W.: The Embryogenesis of Mammalian Blood, in Handbook of Hematology, edited by Hal Downey, New York, Paul B. Hoeber, Inc., 1938, vol. 1.

11. Block, M.: Erythropoiesis in the Embryonic Nervous System of the Rat, Blood **4**: 1156-1167, 1949.

12. Block, M.: The Influence of Intra-Ocular Transplantation upon the Development of the Embryonic Liver of the Rat, Anat. Rec. **103**: 9, 1949.

13. Maximow, A.: The Relation of Blood Cells to Connective Tissues and Endothelium, Physiol. Rev. **4**: 533-563, 1924.

Under a widespread variety of experimental conditions it is possible to stimulate myeloid metaplasia of the spleen and liver. (See reviews by Jordan [8] and Lang.[14]) Of interest from the clinical point of view is the fact that some of these experimental methods such as infections and hemolysins,[14] marrow replacement [15] and irradiation of the marrow with depression of its function [16] resemble the etiologic stimuli which may be present in patients with this syndrome.

This experimentally produced myeloid metaplasia occurs as foci of granulocytes, erythroblasts and megakaryocytes and their precursors in the red pulp of the spleen and in the liver, and to a much lesser extent in lymph nodes, kidney and adrenal. A proliferation of any single cell type or single cell lineage with a distortion of architecture such as is characteristic of leukemia is never found. In this respect experimentally produced myeloid metaplasia and clinical myeloid metaplasia are identical, and both differ from leukemia in man and in animals.[2b]

There is further biologic evidence of the difference between myeloid metaplasia and leukemia. Leukemia has not been caused to occur prematurely and has not even been produced in strains of mice with a high incidence of leukemia by the methods used to induce myeloid metaplasia. If strains of mice in which leukemia may be induced by inoculation of leukemic tissue are inoculated with cells from mice of the same strain with myeloid metaplasia, leukemia will not develop in the former.[17] Barnes and Sisman [17] and Engelbreth-Holm [2b] have outlined the histologic distinctions between leukemia and myeloid metaplasia in mice: the manifestations of myeloid metaplasia that they describe in mice are identical to those seen in patients with myeloid metaplasia of varied causation and of myeloid metaplasia produced experimentally in animals.

MATERIAL

This report is drawn from 12 consecutive cases of myeloid metaplasia diagnosed in the past eighteen months (table 1). In all except 2 instances (cases 1 and 8) the diagnosis was substantiated during life by needle biopsy of the liver or spleen, or both liver and spleen, according to a previously described technic.[18] In the 2 cases in which liver or spleen biopsy was not performed the diagnosis was fairly well substantiated by the bone marrow and peripheral blood studies. To illustrate the frequency with which myeloid metaplasia occurs, in the same period during which these 12 cases were encountered there were 23 cases of myelogenous leukemia seen in this clinic. Admission diagnoses in table 1 indicate in how few cases this diagnosis was made. This observation is especially important because almost all patients had previously had sternal marrow and peripheral blood studies and because patients with myeloid metaplasia usually do poorly after irradiation, splenectomy or nitrogen mustard therapy.

TABLE 1.—*Clinical Observations in Myeloid Metaplasia*

Case	Age	Sex	Symptoms and History	Physical Examination: Liver*	Spleen*	Lymph Nodes	Other	Admitting Diagnoses
1 A. C.	56	F	Polycythemia vera 9 yr., treated by phlebotomies and nitrogen mustard; diarrhea, abdominal pain and weakness 6 mo.	4	12	..	Rumpel-Leede +	Myelogenous leukemia secondary to polycythemia vera
2 M. G.	57	F	Polycythemia vera 4 yr., treated by phlebotomies; intramuscular hemorrhage after needle biopsy of spleen	8	14	..	18 by 20 cm. mass in abdominal muscle	Myelogenous leukemia secondary to polycythemia vera; intraperitoneal hemorrhage following splenic puncture
3 H. M.	58	M	Diarrhea, weight loss and weakness 3 yr.; abdominal mass and occasional bone pain 1 yr.	2	12	..	Osteolytic rib lesions	Aleukemic myelogenous leukemia
4 N. N.	58	M	Diarrhea 3 yr., splenomegaly 1 yr.	0	4	..	.....	Splenomegaly and anemia of unknown causation; mucous colitis
5 G. C.	69	M	Cough 1 yr., weakness 9 mo., dyspnea 3 mo., hemoptysis 1 wk, deafness 4 days	3	4	†	3 cm. density in upper lobe of right lung	Chronic myelogenous leukemia
6 W. S.	68	M	Carcinoma of prostate 4 yr., orchiectomy 1 yr., bone pain 8 mo. and 20 lb. weight loss 4 mo.	3	1	..	Petechia, ecchymoses, osteoplastic and osteoblastic lesions	Carcinoma of prostate with osseous metastases; leukemoid reaction or myelogenous leukemia
7 F. V.	38	F	Weakness 4 mo., weight loss and chest pain 3 mo. Back pain radiating to left knee 6 mo.	0	0	..	Carcinoma of lung by bronchoscopic biopsy	Carcinoma of lung with osseous metastases; leukemoid reaction (leukemia ?)
8 F. W.	28	F	Pain in right upper abdominal quadrant, fever, anemia and splenomegaly 6 wk.	4	20	..	.....	Aleukemic leukemia or Banti's syndrome; fever of unknown origin
9 S. R.	61	F	Pulmonary tuberculosis 10 yr.; cholelithiasis and cholecystectomy 6 yr. ago; 15 lb. weight loss and weakness 18 mo.	0	14	..	.....	Pulmonary tuberculosis; chronic myelogenous leukemia
10 F. Y.	59	F	Stiff joints 9 yr.; weakness, weight loss and splenomegaly 3 yr.	4	20	‡	Advanced flexion deformities of joints	Rheumatoid arthritis; chronic myelogenous leukemia
11 C. B.	54	F	Cough 2 yr.; anemia 1 yr.; 20 lb. weight loss 6 mo.; hemorrhages after dental extraction 2 mo.; jaundice 2 mo.	14	22	..	Icteric, hemorrhagic retinitis	Leukoerythroblastic leukemia
12 P. V.	2½	M	Diarrhea, cough and coryza 6 mo.; anemia and hepatosplenomegaly 3 mo.; multiple allergies	4	5	‡	Xanthomas of skin	Leukemia: xanthomatoses; ulcerative colitis

* Centimeters below costal margin. † Shotty cervical and axillary nodes. ‡ Generalized lymphadenopathy, up to 1 cm.

CLINICAL OBSERVATIONS

The clinical course of patients with myeloid metaplasia has been described.[19] It is obvious from the experience of others as well as our own that in spite of the fairly characteristic history and physical observations the diagnosis can be made only on microscopic grounds.

14. Lang, F. J.: Myeloid Metaplasia, in Handbook of Hematology, edited by Hal Downey, New York, Paul B. Hoeber, Inc., 1938, vol. 3.
15. Steinberg, B.: Tissue Changes in Rabbits with Ablation of Marrow of Long Bones, Proc. Soc. Exper. Biol. & Med. **63**: 393-396, 1946.
16. Jacobson, L. O.; Simmons, E., and Block, M.: The Effect of Splenectomy on the Toxicity of Sr^{89} on the Hematopoietic System of Mice, J. Lab. & Clin. Med. **34**: 1640-1655, 1949.
17. Barnes, W. A., and Sisman, I. E.: Myeloid Leukemia and Non-Malignant Extramedullary Myelopoiesis in Mice, Am. J. Cancer **37**: 1-35, 1939.
18. Block, M., and Jacobson, L. O.: Splenic Puncture, J. A. M. A., **142**: 641-647 (March 4) 1950.
19. (*a*) Favre, M.; Croizat, P., and Guichard, A.: La myélose aleucémique mégacaryocytaire: Contribution à l'étude des syndromes hépatosplénique, Ann. de méd. **35**: 5-43, 1934. (*b*) Hickling.[2b] Paolino.[2c] Rosenthal and Erf.[5]

Study of the history of our patients fails to reveal anything pathognomonic of this syndrome (table 1). Two patients (cases 1 and 2) had polycythemia vera. Myeloid metaplasia has been recognized as a terminal event in this disease.[20] In our opinion the numerous reports that purportedly demonstrate the transition of polycythemia to chronic myelogenous leukemia are based solely on cases with peripheral blood counts without examination of the hematopoietic tissues including liver and spleen [21] or on cases in which myeloid metaplasia was misinterpreted as leukemia.[22] In the cases listed by Blumenthal [23] and Hansen-Pruss and Goodman [24] microscopic examination did not reveal lesions of leukemia in liver, spleen, marrow or kidneys. We have been able to find only 1 case in the literature [25] in which the characteristic histologic observations of chronic myelogenous leukemia were demonstrable in a patient who had polycythemia.

Most of the patients were in the older age group, but our practice is almost entirely limited to adults. By far the commonest complaint was weakness, present as a major complaint in half the patients. This was presumably due to the anemia which was present in all but case 2. Unfortunately, this weak and anemic state, which has been an almost constant characteristic of myeloid metaplasia,[26] occurs in numerous other conditions with which myeloid metaplasia is readily confused.

Three patients had carcinoma and 2 (cases 6 and 7) of these 3 had noted bone pain suggesting the presence of osseous metastases. The combination of carcinoma, abnormal roentgenologic appearance of bone, erythroblasts in the peripheral blood and anemia (cases 5, 6 and 7) is characteristic of myeloid metaplasia.[27] In some cases the erythroblastosis may be so severe and the erythroblastic metaplasia of organs so intense that the "erythroleukemia" of diGuglielmo [7] may be duplicated.[28] None of these 3 patients had roentgenologic changes in the bone similar to those of a mild sclerosing osteomyelitis described by Ducuing and others [29] as being characteristic of diffuse carcinomatosis of the marrow in this syndrome, and only in cases 6 and 7 was the pain severe enough to be a major complaint. One patient with myelosclerosis (case 3) complained of mild pain.

Fever was of major importance in 3 patients (cases 7, 8 and 9) with tuberculosis. They had an acute, miliary type of the disease similar to that seen by others in patients with myeloid metaplasia.[30] The presence of tuberculosis in a patient with a leukemoid peripheral blood picture does not argue in favor of myeloid metaplasia and against leukemia, since tuberculosis may occur in leukemia.[31]

On physical examination the most consistent observation was splenomegaly, which occurred in 11 of 12 patients. Patient 6 without splenomegaly was 1 of the 2 patients in whom the diagnosis of myeloid metaplasia was not verified microscopically by examination of hepatic or splenic tissue. The splenomegaly was extreme, from 12 to 22 cm. below the costal margin in 7 patients and from 1 to 5 cm. below the costal margin in 4 patients. The spleen usually felt firm, was seldom hard and was not painful. Myeloid metaplasia without splenomegaly does occur [2e] but is extremely rare.

The next most commonly observed physical abnormality was hepatomegaly, present in 9 cases. (It was not found in case 7.) The liver was never stony hard or painful, and ascites was never found. The absence of any significant lymphadenopathy was most striking in view of the extremely high incidence of splenomegaly and hepatomegaly. This highly important negative observation has not had sufficient attention called to it, being emphasized only by Hugonot and Sohier,[2d] Jackson, Parker and Lemon [2f] and Hemmeler.[32] In conjunction with splenomegaly and immature red and white cells in the peripheral blood, the absence of significant lymphadenopathy should be considered highly suggestive of myeloid metaplasia.

As noted by Jordan and Scott [2g] and Mendeloff and Rosenthal,[33] a bleeding or bruising tendency was found in almost every patient. This was evident from the history, or by direct inspection, fundoscopic examination, Rumpel-Leede test, platelet count or bleeding and clotting times (tables 1 and 2). It may be severe enough to be the cause of death,[3b] as in cases 1, 2 and 11.

PERIPHERAL BLOOD

Anemia was present in 11 of the 12 patients (table 2). Most patients had about 7 Gm. of hemoglobin, the lowest value being 3.0 Gm. (case 5) and the highest 16 Gm. (case 2). Anemia is practically always present in myeloid metaplasia, except in the occasional patient with polycythemia vera, in whom splenic puncture is performed while he is still in a plethoric state. Myeloid metaplasia is not characteristic of all patients with polycythemia vera; histologic study of the spleen while patients are in an active stage of polycythemia may not

20. (a) Vaughn, J., and Harrison, C. V.: Leuco-Erythroblastic Anemia and Myelosclerosis, J. Path. & Bact. **48**: 339-352, 1939. (b) Hirsch, E. F.: Generalized Osteosclerosis with Chronic Polycythemia Vera, Arch. Path. **19**: 91-97 (Jan.) 1935. (c) Stone, D. M., and Woodman, D.: Polycythaemia Terminating in Leuco-Erythroblastic Anaemia, J. Path. & Bact. **47**: 327-336, 1938.

21. (a) Minot, G. R., and Buckman, T. E.: Erythremia (Polycythemia Rubra Vera). The Development of Anemia; The Relation to Leukemia; Consideration of the Basal Metabolism, Blood Formation and Destruction and Fragility of the Red Cells, Am. J. M. Sc. **166**: 469-489, 1923. Prendergrass, E. P., and Pancoast, H. K.: The Close Relationship of the Erythrogenetic and Leukogenetic Functions of the Bone Marrow in Disease: Report of a Case of Erythremia; The Roentgen-Ray Treatment of Erythremia, ibid. **163**: 797-818, 1922. Heck, F. J., and Hall, B. E.: Leukemoid Reactions of Myeloid Type, J. A. M. A. **112**: 95-101 (Jan. 14) 1939. (b) Rosenthal, N., and Bassen, F. A.: Course of Polycythemia, Arch. Int. Med. **62**: 903-917 (Dec.) 1938. (c) Hall, B. E.; Watkins, C. H.; Hargraves, M. M., and Giffin, H. Z.: Radioactive Phosphorus in the Treatment of Polycythemia Vera: Results and Hematologic Complications, Am. J. M. Sc. **209**: 712-717, 1945. Erf, L. A.: Radiophosphorus as the Treatment of Choice in Primary Polycythemia, Am. J. Med. **1**: 362-366, 1946. Buchanan, G.: Polycythemia Vera (Erythraemia) Terminating in Myelogenous Leukaemia, South African M. J. **19**: 22-23, 1945.

22. Klumpp, T. G., and Hertig, A. T.: Erythremia and Myelogenous Leukemia: Report of Cases Presenting Aspects of Both Diseases, Am. J. M. Sc. **183**: 201-209, 1932. Hirschfeld, H.: Zur Frage der Beziehungen zwischen Erythämie und Leukämie, Folia haemat. **26**: 108-114, 1920.

23. Blumenthal, R.: Sur l'origine myélogène de la polycythémie vraie, Arch. de méd. expér. et d'anat. path. **19**: 697-704, 1907.

24. Hansen-Pruss, O. C., and Goodman, E. G.: Acute Leukemia as a Terminal Event in Polycythemia Vera: Report of 2 Cases wth Autopsies, North Carolina M. J. **4**: 254-258, 1943.

25. Zimmermann, O.: Zur Kasuistik der Erythrämie mit Übergang in Leukämie, Klin. Wchnschr. **13**: 696-699, 1934.

26. (a) Henschen, C., and Jezler, A.: Aleukämische Myelose unter dem Bilde der Panmyelophthise, Ztschr. f. klin. Med. **128**: 343-357, 1935. Hirschfeld.[3a] (b) Paolino.[3c]

27. (a) Chabrol, E.; Cachin, M., and Maurice, P.: L'ostéomyélose diffuse du cancer secondaire des os, Presse méd. **52**: 177-178, 1944. (b) Giraud, G.; Cazal, P., and Maleki, A.: Syndrome ostéo-médullaire diffus d'origine néoplasique: Lésions pagétoïdes; Aplasie médullaire par sclérose; Splénomégalie myéloïde avec érythroblastose sanguine, Sang **18**: 81-89, 1947.

28. Mallarmé and Gorin: L'érythroblastose cancéreuse, Sang **15**: 39-42, 1942-1943.

29. Ducuing, J.; Miletzky, O., and Marques, P.: Document pour l'étude de l'ostéose cancéreuse diffuse et de l'anémie "myélogénétique," Presse méd. **45**: 1693-1695, 1937.

30. (a) Weil, P. E.; Chevallier, P., and Sée, G.: Splénomégalie myéloïde mégacaryocytaire amyélocythémique, Sang **7**: 773-789, 1933. (b) Crail, H. W.; Alt, H. L., and Nadler, W. H.: Myelofibrosis Associated with Tuberculosis: A Report of 4 Cases, Blood **3**: 1426-1444, 1948. Hugonot and Sohier.[3d] Paolino.[3e] Favre, Croizat and Guichard.[3a]

31. Jaffé, R. H.: Tuberculosis and Leukemia, Am. Rev. Tuber. **27**: 32-46, 1933.

32. Hemmeler, G.: Leucémie mégacaryocytaire avec thrombocythémie, J. suisse de méd. **78**: 976-981, 1948.

33. Mendeloff, J., and Rosenthal, J.: Leukoerythroblastic Anemia with Diffuse Osteosclerosis, Ann. Int. Med. **19**: 518-532, 1943.

reveal any evidence of myeloid metaplasia,[2h] and patients who die in the active stage of polycythemia even with immature granulocytes in the peripheral blood may not have myeloid metaplasia.[34]

The height of the white blood cell count was extremely variable in our patients; it ranged from 3,400 to 72,000, illustrating that many patients do not have an elevated white count. Even wider variations in the white count (2,800 [26a] to 227,000 [5]) have been reported. The differential white count was far more significant, since every patient had immature red and white cells in the peripheral blood. One cannot overemphasize that the combination of a grossly elevated white count and a high percentage of immature cells in the peripheral blood, including myeloblasts, is not diagnostic of leukemia.[35] In the case reported by Custer and Crocker [1d] there were 220,000 white cells with 5 per cent myeloblasts and 30 per cent myelocytes, and it was only at autopsy that the diagnosis of leukemia was disproved and that a slight myeloid metaplasia of the spleen was found. We have not found a typical leukemic hiatus to be present in any case of myeloid metaplasia.

Platelet counts were significantly depressed in 6 of the 7 instances in which they were available. The 1 patient with polycythemia in a terminal anemic phase (case 1) had moderate thrombopenia in contrast to the high platelet count characteristic of patients with polycythemia vera. In none of our patients were megakaryocytes observed in the peripheral blood, even though these cells were numerous in the tissues of 3 patients.

HISTOPATHOLOGY

By far the most significant diagnostic aid was biopsy of tissue obtained by needle aspiration of marrow, liver and especially spleen (table 3). Table 3 shows that the marrow cellularity and the extent of myelofibrosis and osteosclerosis was variable from patient to patient and even in the same patient. Three patients (cases 1, 4 and 8) had areas of fibrosis and hyperplasia; 1 patient (case 3) had generalized myelofibrosis and osteosclerosis, and 2 patients (cases 5 and 7) had hypercellular marrows. According to Paolino [3c] about 5 per cent of patients with myeloid metaplasia have hypercellular marrows. However, his figure may not be accurate, since cases without myelofibrosis are often not diagnosed unless splenic or liver tissue is available for microscopic examination. We would like to confirm the finding [36] that unusual numbers of osteoblasts or osteoclasts are not present in fibrous or osteosclerotic marrows in patients with myeloid metaplasia. According to Churg and Wachstein [37] myelofibrosis but not osteosclerosis occurs in about 4 per cent of leukemic marrows at autopsy; therefore the presence of osteosclerosis may be used to rule out leukemia.

TABLE 2.—*Peripheral Blood Data*

Case	Hemoglobin	R. B. C. × 1 Million	W. B. C. × 1,000	Platelets × 1,000	Retics. per 1,000 R. B. C.	Differential: Neutrophils	Lymphocytes	Monocytes	Eosinophils	Basophils	Metamyelocytes	Myelocytes	Promyelocytes	Myeloblasts	Normoblasts per 100 W. B. C.	Bl. Time (Sec.)	Cl. Time (Sec.)
1	7.1	3.1	12	146	...	65	11	1	..	1	14	6	1	1	10	13	..
2	16.0	7.0	72	...	...	70	5	2	3	0	13	7	0	0	..	2	..
3	8.1	2.3	3	253	...	38	20	0	3	3	15	9	8	4	14	11	15
4	10.2	3.2	6	...	4.3	70	23	1	2	3	1	0	0	0	5	..	..
5	3.8	0.3	54	...	...	59	5	13	0	1	9	3	1	9	6	..	..
6	7.0	2.6	7	129	8.0	53	3	6	..	..	24	14	..	..	10	6	10
7	8.7	2.8	5	93	1.0	46	29	5	1	..	9	10	..	..	5	10	20
8	10.2	3.2	6	...	4.3	70	23	1	2	3	1	..	..	..	5	..	..
9	9.8	2.7	7	129	3.8	53	3	7	..	..	24	13	..	..	10	6	10
10	7.2	2.7	52	...	...	79	7	3	1	..	1	5	2	2	2	..	..
11	7.3	1.8	52	82	15.5	43	5	14	1	4	15	12	1	5	279	25	36
12	9.0	3.9	17	30	2.4	43	45	3	..	..	7	2	..	1	1	7	..

Every patient (except in case 2) had nucleated red cells in the peripheral blood. In 8 patients there were between 5 and 14 normoblasts and in one 279 normoblasts, per 100 white cells. Practically all normoblasts were mature with eosinophilic cytoplasm, but in case 12 the peripheral smear disclosed as many immature nucleated red cells as the average patient has in the bone marrow, the erythroblastic hiatus of diGuglielmo's [7] "erythroleukemia." The simultaneous occurrence of immature cells of the red and white series is of utmost diagnostic importance in the separation of myeloid metaplasia and leukemia,[1a] especially if the increase in erythroblasts is greater than that commonly seen in leukemia, since erythroblasts may also be seen in the peripheral blood of the latter disease.[2c] In general, reticulocytosis runs parallel to the normoblastosis, and in this series reticulocytes were increased in number in 6 of 7 patients on whom counts were available.

The presence of a fibrous marrow or of areas of fibrous and hyperplastic marrow is of importance from a practical point of view. In 6 of the 12 patients at least one marrow aspiration failed to produce enough cells to make an adequate smear for diagnosis. In case 3 two sternal aspirations were unsuccessful. Aspiration of marrow in case 4 resulted in an extremely acellular smear, although sections of aspirated particles revealed a mixed cellular and fibrous marrow. A similar observation, an acellular smear and hypercellular sections, was made in cases 5, 8 and 10. Our results

34. Rosenblum, M. B., and Kremer, D. J.: Zur Frage über eine Kombination von Leukämie and Erythrämie, Folia haemat. **41**: 484-492, 1931. Blumenthal.[29]

35. (*a*) Downey, H.; Major, S. G., and Noble, J. F.: Leukemoid Blood Pictures of the Myeloid Type, Folia haemat. **41**: 493-511, 1930. Krumbhaar, E. B.: Leukemoid Blood Pictures in Various Clinical Conditions, Am. J. M. Sc. **172**: 519-533, 1920. (*b*) Thompson, W. P.: Abnormalities in the White Blood Cell Response: Leukemoid, Atypical Leukemic and Leukopenic Blood Pictures, ibid. **182**: 334-352, 1931. (*c*) Rosenthal and Erf.[5]

36. (*a*) Windholz, F., and Foster, S. E.: Bone Sclerosis in Leukemia and Non-Leukemic Myelosis, Am. J. Roentgenol. **61**: 61-76, 1949. (*b*) Erf, L. A., and Herbut, P. A.: Primary and Secondary Myelofibrosis (a Clinical and Pathological Study of 13 Cases of Fibrosis of the Bone Marrow), Ann. Int. Med. **21**: 863-889, 1944.

37. Churg, J., and Wachstein, M.: Osteosclerosis, Myelofibrosis and Leukemia, Am. J. M. Sc. **207**: 141-152, 1944.

therefore serve to emphasize that in fibrous marrows [38] and marrows with carcinomatosis [27b] smears of marrow aspirates may be exceedingly misleading or not productive of sufficient tissue for diagnosis. An acellular smear in a patient suspected of having leukemia should immediately raise the suspicion of myeloid metaplasia, and surgical excision of tissue for biopsy should be performed. In the patient (case 3) with the most fibrosis of the marrow surgical excision was necessary to obtain adequate tissue for study.[39] In the marrows that were hyperplastic the erythroblast was the dominant cell, a condition which is clearly not characteristic of the marrow in leukemia.

Extramedullary hematopoiesis was present in the livers of each of the 6 patients who were subjected to hepatic puncture. The myeloid metaplasia was primarily erythroblastic, although in cases 4 and 8 there were tremendous numbers of megakaryocytes. There was extramedullary hematopoiesis in most patients in portal areas as well as in the sinusoids. In case 8 caseating granulomas were found in the liver biopsy and puncture it is probable that the white pulp was not included in the specimen rather than that the spleen did not have white pulp. In most biopsies the white pulp was decreased in amount, but a decrease in the amount of white pulp is common in the older age group.[42] The splenic cords and sinuses were well demarcated (table 3). Myeloid metaplasia with active erythropoiesis was found in each case examined. In no spleen was there an effacement of the architecture due to proliefration of a single cell type or single cell lineage that is so characteristic of leukemia [43] and that we have observed in biopsies of spleens in our patients with leukemia.[44] The microscopic picture in these spleens derived from patients with myeloid metaplasia of varied causation resembled much more closely what Engelbreth-Holm [2b] and Barnes and Sisman [17] have described in myeloid metaplasia rather than in leukemia in mice. In Hirschfeld's comprehensive review [3a] this histologic pattern was classified as belonging to leukemia, although he admitted that it is atypical for leukemia. He stated that tuberculosis, carcinomatosis

TABLE 3.—*Histologic Observations* (Tissues Obtained by Biopsy)*

	Liver				Spleen			Marrow	
		Lobular			Red Pulp				
Case	Portal	E	G	M	E	G	M	Smear	Section
1	.....	...	...	...	...	...	...	Q. N. S.	Fibromyxomatous islands of giant cells and active marrow
2	1+ F†	2+	...	1+	2+	?	2+	.....	4+ C, 4+ M
3	.....	1+	...	4+	2+	3+	1+	Q. N. S. twice	Fibromyxomatous
4	.....	...	...	1+	4+	4+	2+	Q. N. S. once; E hyperplasia second time	Hyperplastic, occasional fibrotic areas
5	3+ F 3+ L	4+	1+ 3+ iron pigment	...	2+	4+ 2+ plasma cells	...	Q. N. S.	4+ C; nests of cancer cells
	3+ G	...	...	...	...	...	...		
6	1+ G	4+	1+	r	...	...	...	E. hyperplasia	4+ cells; mainly E
7	.....	...	...	...	...	...	...	Subacute myelogenous leukemia? cancer?	Metastatic carcinoma
8	1+ F 1+ L	1+	rare caseating tubercles	4+	1+	2+ 2+ plasma cells	4+	Q. N. S. twice	Fibromyxomatous, islands of active marrow; 4+ M
9	*	1+	...	1+	3+	1+	1+	4+ E	4+ cell, primarily E
10	* r G	4+	1+ occasional plasma cell	r	1+	3+	r	Q. N. S. once; E hyperplasia	4+ C, 3+ E, 2+ G, 1+ M
11	1+ G	4+	1+	...	4+	1+	1+	Cellular	4+ C, primarily E
	.....		4+ iron pigment		...	...	...		
12	.....	...	...	...	2+	4+	1+	G hyperplasia	.....

* The letter L denotes lymphocytes; G, granulocytes precursors; E, erythroblasts, and M, megakaryocytes; F denotes fibrosis; C, cellularity, r, rare, and Q. N. S., insufficient material on aspiration. † Liver tissue obtained at autopsy.

not in either of 2 splenic punctures. In no case was the metaplasia primarily granulocytic.

Microscopic examination of splenic tissue (table 4) is the most important step in diagnosis,[40] which may be impossible without this procedure. We are at a loss to understand how examination of tissue obtained by splenic puncture has failed to reveal the diagnosis in the case reported by Levinson and Limarzi.[41] It is possible that an inadequate preparation was obtained if only smears were examined.[18]

In almost every case the white pulp was clearly demonstrable. In those cases in which white pulp was not demonstrable in the specimen obtained by splenic and the various experimental means of producing myeloid metaplasia result in a histologic state which is much more similar to that seen in patients with myeloid metaplasia than with leukemia.

Cases 3 and 8 were characterized by extremely numerous megakaryocytes in the liver and spleen. Unlike Weil and associates,[45] Hugonot and Sohier [2d] and Favre, Croizat and Guichard,[10a] we do not consider this sufficient evidence to classify the 2 cases separately as cases of megakaryocytic leukemia. Nor do we believe that those cases with fever and an acute course (such as our case 12) in which erythroblasts are numerous and preponderant should be classified in a special group as cases of erythroblastic leukemia,[46] since identical conditions occur in patients with carcinomatosis.[47] As had

38. Mettier, S. R.: Hematologic Aspects of Space Consuming Lesions of the Bone Marrow (Myelophthisic Anemia), Ann. Int. Med. **14**: 436-448, 1940. Thompson and Illyne.[1a] Jackson, Parker and Lemon.[2f] Rosenthal and Erf.[3] Engell.[6] Erf and Herbut.[26b]

39. The slide was loaned by Dr. Malcolm Hargraves of the Mayo Clinic, Rochester, Minn.

40. (*a*) Forconi, A.: Pour confirmer l'importance des ponctions de la rate et de la moelle osseuse dans les myéloses érythrémiques sub- et aleucémiques, Sang **13**: 380-392, 1939. Reich and Rumsey.[6a] (*b*) Hugonot and Sohier.[2d] Jackson, Parker and Lemon.[2f] Weil, Isch-Wall and Perlès.[3b]

41. Levinson, S. A., and Limarzi, L. R.: Agnogenic Myeloid Metaplasia of the Spleen: Report of a Case with Necropsy Findings, Am. J. Clin. Path. **17**: 449-461, 1947.

42. Andrew, W.: Age Changes in the Vascular Architecture and Cell Content in Spleens of 100 Wistar Institute Rats, Including Comparisons with Human Material, Am. J. Anat. **79**: 1-73, 1946.

43. Moeschlin, S.: Die Milzpunktion, Basel, Benno Schwabe, 1947.

44. Block, M., and Jacobson, L. O.: Unpublished material.

45. Weil, Isch-Wall and Perlès.[2b] Weil, Chevallier and Sée.[30a]

46. Harvier, P.; Le Melletier, J.; Lavergne, G. H., and Lamotte, M.: Érythroleucomvélose aiguë. Sang. **15**: 272-278, 1942. Weil, Isch-Wall and Perlès.[3b] diGuglielmo.[7] Levinson and Limarzi.[41]

47. Chabrol, Cochin and Maurice.[27a] Giraud, Cazal and Maleki.[27b] Mallarmé and Gorin.[26]

been pointed out,[48] these are all essentially the same disease although in any one person one or the other of three cell lineages normally found in the marrow may be increased out of proportion to the others. It is important that no one of these cell lineages is hyperplastic enough or distorts the fundamental architecture of the spleen sufficiently to warrant a diagnosis of leukemia and that they may occur idiopathically or secondary to carcinomatosis or tuberculosis.

DIFFERENTIAL DIAGNOSIS

Reference to table 1 will demonstrate that the error most commonly made was confusion of myeloid metaplasia with various types of leukemia. In table 4 the similarities and in table 5 the differences between the two are delineated. Splenic biopsy or liver biopsy may be needed to differentiate between these two diseases. We recently erroneously diagnosed 1 case of subacute myelogenous leukemia as myeloid metaplasia because of the presence of an unusually large number of erythroblasts in the spleen and liver and some slight degree of preservation of splenic architecture. The bone marrow of this patient was characteristic of subacute myelogenous leukemia. It is therefore impossible to be dogmatic about the differential diagnosis, but in the great majority of cases leukemia and myeloid metaplasia may be distinguished histologically.

Other conditions to be considered in the differential diagnosis are the common causes of hepatosplenomegaly and of splenomegaly with anemia such as Banti's syndrome, splenic neutropenia and idiopathic thrombopenic purpura, leukemoid reactions, fat storage disease, splenic anemias and infectious granulomas such as tuberculosis and histoplasmosis. To confuse the issue, generalized tuberculosis is one of the commoner causes of myeloid metaplasia. The hemorrhagic tendency may be severe enough to simulate aplastic anemia[32] or purpura.[35b] These diseases seldom have the combination of a leukemoid blood picture with normoblastosis. However, the most nearly certain method of diagnosis is still needle biopsy of the spleen and liver and examination of sections of the bone marrow.

CLASSIFICATION

Myeloid metaplasia may be divided into two general types, primary (without a known etiologic basis) and secondary. The primary type usually has an exceedingly active marrow in which normoblasts predominate and which never has the shift to the left and the overwhelming of the marrow by granulocytic precursors that are seen in myelogenous leukemia. Cases 4, 10, 11 and 12 belong to this category.

Secondary myeloid metaplasia occurs with lesions of the bone marrow such as metastatic carcinoma[27] (cases 5, 6 and 7), marble bone disease[36b] and myelofibrosis or osteosclerosis[5] (cases 1 and 3) as well as with tuberculosis[48b] (cases 8 and 9). Osteosclerosis may be idiopathic or may represent a terminal stage in polycythemia rubra vera.[20] True persistent myeloid metaplasia is rare after infections in spite of the frequency of leukemoid reactions and transitory myeloid metaplasia after infection. It is of greatest importance that the histologic picture is essentially similar regardless of the etiologic basis of the myeloid metaplasia.

48. (*a*) Waitz, R., and Warter, J.: Contribution à l'étude des myéloses aleucémiques: Splénomégalie myéloïde, érythroblastique et mégacaryocytaire; Mégacaryocytose et sclérose de la moelle osseuse; Splénectomie, Ann. de méd. **44**: 344-364, 1938. (*b*) Carpenter, G., and Flory, C. M.: Chronic Nonleukemic Myelosis: Report of a Case with Megakaryocytic Myeloid Splenomegaly, Leukoerythroblastic Anemia, Generalized Osteosclerosis and Myelofibrosis, Arch. Int. Med. **67**: 489-508 (March) 1941. Paplino.[c] (*c*) Vaughn and Harrison.[36a] Erf and Herbut.[36b]

PROGNOSIS

The duration of life of the patient after diagnosis of myeloid metaplasia or beginning with the onset of symptoms or of splenomegaly is variable. Patients in whom the disease begins as polycythemia may live as long as twenty-three years, but they succumb within a relatively short time once an anemic stage is reached.[49] In most patients with the nontuberculous and noncancerous types of myeloid metaplasia the disease has a chronic course of thirty to thirteen years,[50] although in about 5 per cent, particularly those with hyperplastic marrows, it may run an acute, almost septic course.[51] With cancerous metastases and tuberculosis the disease has an extremely acute course.

TABLE 4.—*Characteristics Observed in Myeloid Metaplasia and Leukemia*

History
May be primary disease
Bleeding and bruising
Weakness due to anemia
Presence of tuberculosis
Fever, anorexia and weight loss
Physical
Splenomegaly and/or hepatomegaly
Purpura and ecchymoses
Positive Rumpel-Leede test
Laboratory
High, low or normal total white blood cell count
Immature cells in peripheral blood
Thrombopenia
Anemia
Pathology
Extramedullary hematopoiesis
Iron deposits in liver (secondary hemochromatosis)

TABLE 5.—*Differentiation Between Myeloid Metaplasia and Leukemia*

	Myeloid Metaplasia	Leukemia
	History	
	Other primary disease (tuberculosis, polycythemia, carcinoma)	Primary
	Physical	
Lymphadenopathy	Usually insignificant	Usually pronounced
Fever	Infrequent without tuberculosis	Frequent when active
	Peripheral Blood	
Normoblasts in peripheral blood	Invariable and may be numerous	Infrequent and not numerous
Immature cells	Left shift moderate	More pronounced shift to the left
Leukemic hiatus	Absent	May be present
	Pathology	
Spleen		
Architecture	Preserved	Destroyed or decidedly altered
White pulp	Atrophic	Absent or decidedly reduced
Megakaryocytes	Usually present, may be very numerous	Rare or absent
Erythroblasts	Numerous	Rare or absent
Lymph nodes		
Architecture	Preserved	Obscured
Metaplasia	Slight or absent	Pronounced
Marrow specimen	May be difficult to obtain surgically	Cellular specimens obtained by aspiration
Cellularity	Atrophic to hypercellular	Almost always hypercellular
Erythroblasts	Numerous	Rare
Megakaryocytes	At least normal	Decreased except in early myelogenous leukemia
Liver		
Erythroblasts	Always present	Rare
Megakaryocytes	Almost always present	Rare
Other organs	Little involvement	May have massive metaplasia in kidney, heart, skin and adrenal

49. Hirsch.[39b] Stone and Woodman.[39c] Rosenthal and Bassen.[21b]

50. (*a*) Picard, R.; Horeau, J., and Kerneis: Myélose splénomégalique hypoleucémique évoluant dupuis plus de 13 ans, Sang **18**: 121-124, 1947. (*b*) Heller.[3c] Windholz and Foster.[36a]

51. Paolino.[3c] Heller.[3c]

TREATMENT

The general consensus is that in myeloid metaplasia splenectomy [52] and irradiation of the spleen are contraindicated.[40a] It would appear that splenectomy or splenic irradiation might deprive the patient with myelofibrosis or osteosclerosis of myeloid tissue which is attempting to compensate for a deficient marrow. In spite of the dominant opinion today, Reich and Rumsey [48] reported that a patient lived five years after splenectomy and Picard, Horeau and Kerneis [50a] that a patient lived thirteen years even though given frequent courses of irradiation therapy. Our own cases have been followed for so short a time that we can only verify the fact that patients with tuberculosis (cases 9 and 10), exceedingly hyperplastic marrows (case 12) and in the anemic phase of polycythemia (case 1) lived only a matter of months after the onset of myeloid metaplasia.

Other types of therapy such as testosterone,[36b] liver and iron [20c] and nitrogen mustard [32] have been used but do not seem to have been particularly effective. In particular nitrogen mustard seems contraindicated judging from Hemmeler's experience.

CONCLUSIONS

1. Evidence is presented that in adult mammals there are tissues in the liver and spleen capable of producing cells normally formed in the marrow.

2. Common characteristics of myeloid metaplasia are weakness, hemorrhagic tendency, splenomegaly, hepatomegaly, a leukemoid peripheral blood with normoblastosis and a specific type of myeloid metaplasia of the spleen and liver. Myeloid metaplasia of lymph nodes, kidney and adrenal is rarer and occurs to only a slight extent.

3. The peripheral blood may have a high, low or normal white cell count with large numbers of immature granulocytes, a condition identical to that seen in leukemia.

4. The bone marrow may be fibrotic, hyperplastic or the site of carcinomatous metastases. An unsuccessful or cell-poor marrow aspiration in a patient should always make one suspect the validity of the diagnosis of leukemia and is an indication for surgical excision of tissue for biopsy if a second aspiration is also unsuccessful.

5. The diagnosis and especially the differentiation from leukemia may be established only by means of biopsy of liver or spleen. Accurate diagnosis is important because splenectomy and splenic irradiation or other forms of treatment commonly used in leukemia are contraindicated.

6. The prognosis is best in patients with fibrous marrows and poorest in patients with hyperplastic marrows or marrows that are the site of carcinomatous metastases or in patients with widespread tuberculosis.

7. Myeloid metaplasia is regarded as a nonspecific response of immature multipotent cells of the liver and spleen to a wide variety of stimuli and is of a fundamentally different nature than leukemia.

8. The histologic and clinical manifestations of this syndrome are essentially the same regardless of the varied etiologic factors which may be the cause of myeloid metaplasia.

52. Mettier and Rusk.[1c] Rosenthal and Erf.[8]

PATHOGENESIS OF URTICARIA

Experimental Study of Life Situations, Emotions and Cutaneous Vascular Reactions

DAVID T. GRAHAM, M.D.
and
STEWART WOLF, M.D.
New York

The association of urticaria with stressful life situations has been observed by numerous authors,[1] but there are few available data concerning the mechanisms involved. Grant, Pearson and Comeau,[1b] who studied the urticaria that occurs with exercise, warming of the body and "emotion," found that parasympathomimetic drugs produced urticaria in susceptible persons. Hopkins, Kesten and Hazel [1c] confirmed these observations. They inferred that urticaria in their patients represented an allergic reaction to acetylcholine released at nerve endings during the resulting vasodilatation.

Lewis [2] demonstrated the importance of cutaneous vascular changes in the production of wheals. Accordingly, in our investigation measurements of blood vessel function were correlated with changes in the life situation, attitude and feeling state in 30 patients with chronic urticaria. Three procedures were employed: Life history material was correlated with the appearance and subsidence of symptoms; material thought to be symptom provoking was deliberately introduced during interviews and resulting skin changes were measured; response to vasodilating agents in the patients was studied and compared with that of a control group.

MATERIALS AND METHODS

Patient Population and Interview Procedure.—Thirty subjects, 17 women and 13 men, who had had repeated attacks of urticaria or whose present attack had lasted three weeks or longer were studied. The patients were otherwise unselected. The lesions varied from superficial wheals 2 to 3 mm. in diameter to deep-seated swellings 15 cm. in diameter. A single subject often displayed different kinds of lesions at different times. Almost every one of the patients had at one time or another diffuse swellings on the face and neck, or about the joints, characteristic of angioneurotic edema. Several had little spontaneous whealing but had chronic itching with blotchy erythema of the skin and pronounced dermographism.

The subjects were followed in the clinic until they recovered or discontinued treatment. All those seen for a total of two hours or longer have been included in the series. Except for the occasional administration of antihistaminic agents for the relief of symptoms, treatment involved only a consideration of life situations and the patients' reactions to them. They were urged to eat unrestricted diets and to lead unrestricted lives.

From the New York Hospital and the Department of Medicine of Cornell University Medical College.

Read before the Association for Research in Nervous and Mental Diseases, Dec. 3, 1949, New York. To be printed in full with case reports as part of the Proceedings of that association.

1. (a) Dunbar, F.: Emotions and Bodily Changes: A Survey of Literature on Psychosomatic Interrelationships, 1910-1945, ed. 3, New York, Columbia University Press, 1947. (b) Grant, R. T.; Pearson, R. S. B., and Comeau, W. J.: Observations on Urticaria Provoked by Emotions, by Exercise and by Warming the Body, Clin. Sci. **2**: 253-272, 1936. (c) Hopkins, J. G.; Kesten, B. M., and Hazel, O. G.: Urticaria Provoked by Heat or Psychic Stimuli, Arch. Dermat. & Syph. **38**: 679-691 (Nov.) 1938. Saul, L. J., and Bernstein, C., Jr.: The Emotional Settings of Some Attacks of Urticaria, Psychosom. Med. **3**: 349-369, 1941. Stokes, J. H.; Kulchar, G. V., and Pillsbury, D. M.: Effect on the Skin of Emotional and Nervous States: Etiologic Background of Urticaria with Special Reference to Psychoneurogenous Factor, Arch. Dermat. & Syph. **31**: 470-499 (April) 1935.

2. Lewis, T.: The Blood Vessels of the Human Skin and Their Responses, London, Shaw and Sons, Ltd., 1927.

In each case a relatively complete life history was obtained with particular reference to an understanding of the setting in which the first and subsequent urticarial attacks occurred. An important part of such understanding was a knowledge of the patient's feelings about the situation and his general behavior with respect to it. Note was made of foods ingested and exposure to other possible allergens.

In the experimental setting and after suitable control observations significant topics, known to have been associated in the past with outbreaks of urticaria, were brought up for discussion and dwelt on for several minutes. The aim was to arouse in the patient the same emotional state as that which had been associated with the events when they actually occurred. The experiment concluded with a period of strong reassurance and diversion. During the entire procedure we determined the skin temperature and the reactive hyperemia threshold (discussed later) at varying intervals, making certain that readings were always obtained when there was a major shift in the material discussed or when the patient showed signs of emotion by his voice, skin color or gestures. He was afterward questioned carefully to check the data about his feelings and reactions during the various phases of the experiment.

The questioning of the patient was aimed at determining how he perceived the traumatic situation and what his response tendencies were. If the patient did not give this information spontaneously, he was asked specifically to describe the nature and presumed intent of the action taken by other persons involved and his own plans, if any, for dealing with it. When clearcut answers were not obtained in this way, he was offered several alternative descriptions of stressful situations and asked to choose one from among them. He was then asked what action he had wished or intended to carry out himself. It was emphasized that information was sought only concerning the period when urticaria was occurring, since the same situation might appear in different lights at different times. Every effort was made to avoid suggesting answers, and it was hoped that dealing with the reports of a patient in this way would eliminate some of the problems encountered in treating such material objectively. Only infrequently was there difficulty in obtaining unequivocal statements from a patient after he understood what information was being sought.

Measures of Cutaneous Vascular Function.—The skin temperature and the reactive hyperemia threshold (discussed later) were employed as measures of cutaneous vascular function, since they reflect the activity of the arterioles and the minute vessels, respectively. It is important to consider these two distinct types of blood vessels separately because they may act independently and they determine different aspects of cutaneous reaction. The arterioles, as the site of most of the peripheral resistance to blood flow, control the cutaneous flow and hence determine the hue of the skin—blueness or redness—because the degree of hemoglobin reduction is a function of, among other things, the rate of flow, which also is a major factor determining skin temperature. The minute vessels, the capillaries and venules, which need not for present purposes be further distinguished, control the saturation of skin color; when they are constricted the skin is pale, no matter what the total blood flow may be. They may also have some effect on the skin hue, since the size of the capillary bed will affect the linear velocity of flow, independently of the influence of the arterioles on the quality of blood delivered per unit time. In these smaller vessels there occurs the exchange of fluid and solutes with the tissue.[3]

In the triple response of Lewis both kinds of vessels are dilated. The dilated minute vessels are responsible for the "red reaction" and dilated arterioles for the "flare." Lewis believed that it was necessary to postulate a third factor to account for increased capillary permeability and wheal formation, but his arguments are not conclusive in view of the probability, according to Ponder,[4] that a dilated capillary is *ipso facto* a more permeable one. Since dilatation of arterioles reduces the usual pressure drop in the blood passing through them, thereby raising the intracapillary pressure, wheal formation may be viewed as the result of increased transudation of fluid consequent to increasing the pressure in a dilated and therefore more permeable capillary.

In the present study, skin temperature as an indicator of the caliber of the arterioles was measured with a Hardy radiometer.[5] The state of the minute vessels, on the other hand, was assessed by measurement of the reactive hyperemia threshold, according to the method of Di Palma, Reynolds and Foster.[6] This is a test of tonus—that is, of resistance to dilatation, and not of the actual caliber of the vessels. The test consists of applying a weight to the skin long enough to produce, after it is removed, a change in intensity of skin color, i. e., a zone of erythema due to minute vessel dilatation. The end point of the test is that length of time required to produce a complete ring of hyperemia in the skin without spread of erythema to skin on which the weight was not resting. If minute vessel tone is low, the time required is short; if the time required is long, tone is high. All measurements were made on the skin of the ventral surface of the forearm. The experiments were performed at room temperatures varying between 22 and 28 C. The temperature of the room in each experiment was maintained constant. Rarely it varied as much as 1.5 degrees during any single experiment. When there was evidence that skin temperature changes might be reflecting changes in the environmental temperature the observations were omitted from consideration.

In addition to the measurements made during experimental interviews, sensitivity of the skin to histamine and pilocarpine introduced by iontophoresis was determined in 24 of the patients and in 24 controls, of whom 20 were healthy hospital personnel and 4 were patients without skin disease. One square centimeter of Canton flannel was saturated with the solution being tested, and a current of 100 microamperes was allowed to flow for two minutes. The active electrode was a square of aluminum foil. The solutions employed were histamine acid phosphate 0.001 per cent and pilocarpine hydrochloride 1 per cent. In a few persons, the response of the skin to warming the body by soaking the legs in water at 43 to 45 C. and to the intramuscular injection of 6 mg. of pilocarpine hydrochloride was also investigated.

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3. (*a*) Edwards, E. A., and Duntley, S. Q.: The Pigments and Color of Living Human Skin, Am. J. Anat. **65**: 1-33, 1939. (*b*) Lewis,[2] Weiss, S.; Robb, G. P., and Ellis, L. B.: The Systemic Effects of Histamine in Man with Special Reference to the Responses of the Cardiovascular System, Arch. Int. Med. **49**: 360-396 (June) 1932.

4. Ponder, E.: The Capillaries and the Lymphatics, in Howell's Textbook of Physiology, edited by John Fulton and others, ed. 15, Philadelphia and London, W. B. Saunders Company, 1949.

5. Hardy, J. D., and Soderstrom, C. F.: An Improved Apparatus for Measuring Surface and Body Temperature, Rev. Scient. Instruments **8**: 419-422, 1937.

6. Di Palma, J. R.; Reynolds, S. R. M., and Foster, F. S.: Quantitative Measurement of Reactive Hyperemia in Human Skin, Am. Heart J. **23**: 377-389, 1942. Dr. Di Palma made available two of the weighted rings used in the test.

RESULTS

Relation Between Life Situations and Symptoms.—In 29 of the 30 cases there was an almost invariable relationship between an attitude of a particular kind and attacks of urticaria. The single exception was a girl who made only two visits to the clinic, and even in

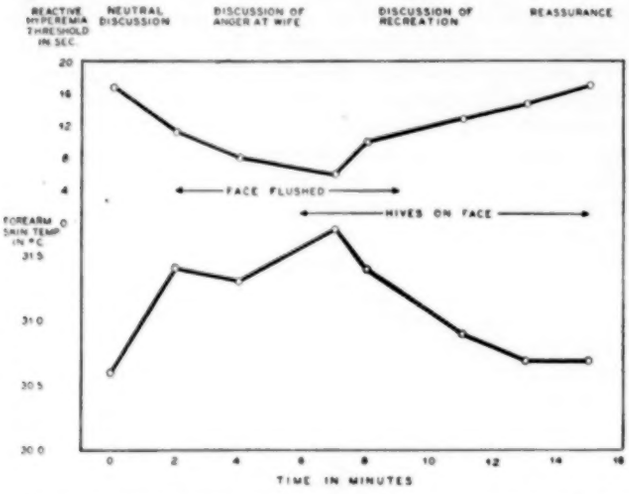

Fig. 1.—Vascular changes in the forearm skin of a male patient during an interview in which he expressed resentment of his wife and urticarial lesions developed on his face.

her it was possible to identify the particular emotional pattern seen in the others, but it was not possible in the limited time available to correlate attacks temporally with these feelings. In brief, these patients considered themselves wronged or injured (usually by someone in a fairly close family relationship), and they regarded the traumatizing situation as one which precluded any action on their parts. They believed that they could neither retaliate nor run away. In this setting they became intensely resentful, and urticaria developed.

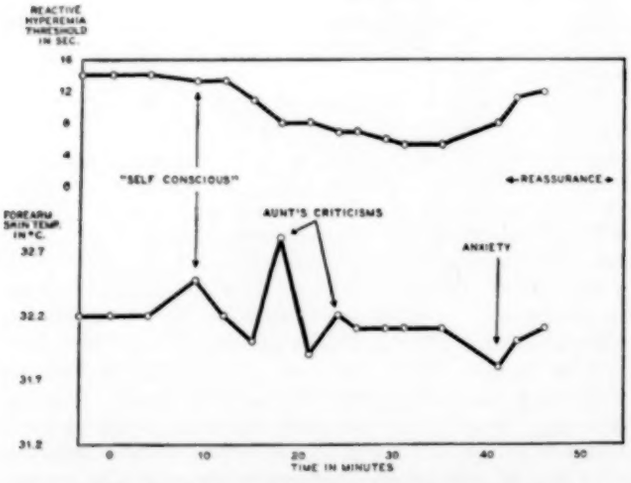

Fig. 2.—Vascular changes in forearm skin of one young man during interview. The two rises in skin temperature which occurred while he was discussing his aunt were both in connection with her criticism of him; the intervening drop was associated with his remarks about other phases of her life. The changes occurring when anxiety about his academic success developed at the end of the interview are seen to contrast with those during a period of resentment.

Emotions of anxiety, hostility, grief or dejection were not directly associated with attacks of urticaria, though many of the patients experienced some or all of these feelings at various times, in addition to resentment. In no instance was any important correlation discovered between exposure to foods or other substances commonly thought of as allergens and attacks of the disease. Detailed case reports will be published elsewhere.[7]

VASCULAR CHANGES DURING STRESSFUL INTERVIEWS

All the subjects were seen to flush when topics of significant personal concern were brought up for discussion. The flush was usually blotchy and of varying intensity, but it often extended at least as far as the waist and wrists. Five subjects had urticarial lesions while discussing their problems. In 20 of the patients the reactive hyperemia threshold was followed during interviews on one or more occasions. When resentment was aroused by a discussion of events which in the past had been associated with attacks of urticaria, capillary tone was invariably lower than during control periods. Moreover, in persons whose urticaria developed during interviews the reactive hyperemia threshold was low while lesions were appearing.

In 13 cases measurements of forearm skin temperature were made. In all subjects who became resentful, it rose at the same time that minute vessel tone was

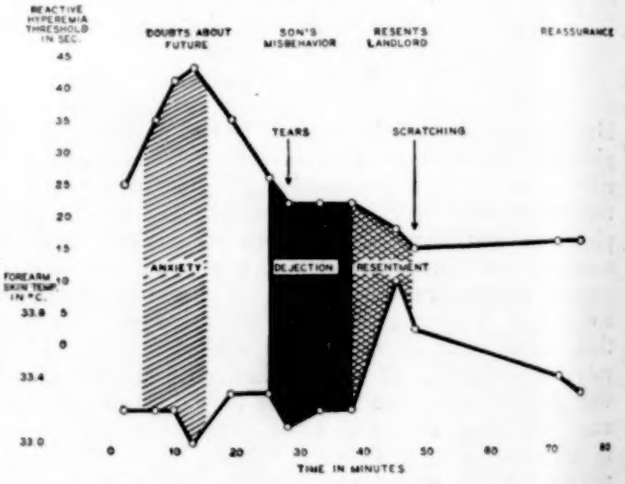

Fig. 3.—Experimental interview with a woman, during which she expressed anxiety about the future, dejection about the impossibility of any improvement in her son and resentment of her landlord.

decreased. One person who discussed his problems without any indication of distress did not have significant changes in skin temperature. The skin temperature of another failed to rise when the interview elicited only grief and dejection, accompanied with weeping. Figure 1 illustrates a typical interview. For orientation with respect to this and subsequent illustrations, it will be seen that movement of either line toward the center of the chart represents dilatation of the vessels concerned, while movement away from the middle represents constriction.

It should be noted that the persons studied did not show this pattern of dilatation of both arterioles and minute vessels in all circumstances. Figures 2 and 3 indicate that when chiefly anxiety is experienced, the minute vessels gain tone and the arterioles constrict. Associated with predominant feelings of dejection and hopelessness there was a loss of minute vessel tone but a lowered skin temperature, probably indicating arteriolar constriction (fig. 3). This conforms with the clinical experience that these emotional states are not associated with attacks of urticaria. When the inter-

7. Graham, D. T.: The Pathogenesis of Hives, Proc. A. Research Nerv. & Ment. Dis. **29**: 1950, to be published.

view was not stressful significant changes were not noted (fig. 4). In 1 subject (fig. 5) it was possible during a stressful interview to demonstrate simultaneous changes in the response of the skin to histamine, to pilocarpine and to stroking. The minute vessel tone was low when it was measured at the height of skin reactivity, and it increased as response to the other stimuli decreased. In 2 other subjects similar changes in the response to stroking during a single interview were observed.

SENSITIVITY TO VASODILATING STIMULI

Every one of the patients with urticaria manifested dermographism (wheal formation in response to a single moderately strong stroking of the skin), although in some this was not apparent until stressful interviews had altered the state of their skin vessels. "Spontaneous" lesions often occurred at sites of mild mechanical trauma, such as under belts, collars, shoulder straps and wrist watch straps.

Iontophoresis skin tests were performed on 24 of the patients, without any effort being made to induce resentment at the same time: 23 of them responded with at least some whealing to histamine, and 23 responded with whealing to pilocarpine. Isotonic sodium chloride solution applied in the same way gave rise to whealing in only 1 patient, and the response was much less than that to the other two solutions. In 2 cases the test to pilocarpine was negative on the ventral surface of the forearm, where the subjects concerned never had lesions, but was positive on the chest and thigh, respectively, where lesions often did occur.

In 25 control subjects, response to histamine was seen in only 6 and to pilocarpine in only 3. Attempts to provoke urticaria by soaking the legs in hot water were successful in 3 of the 4 patients in whom the procedure was tried. In 1 of the 4 lesions developed over most of the body surface. These began to recede promptly when atropine sulfate was injected, corresponding to the experience of Grant, Pearson and Comeau.[1b] The injection of pilocarpine was followed by the appearance of wheals at different sites in 4 of 8 patients. Both procedures resulted in marked flushing of the skin in all patients tested.

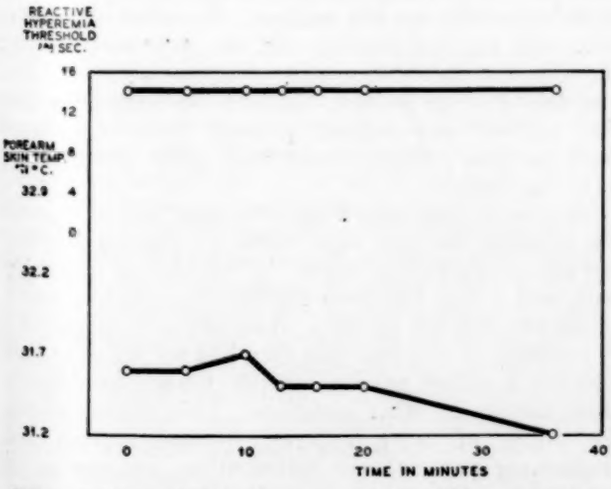

Fig. 4.—Relative stability of measures of cutaneous vascular function during a nonstressful interview with the patient whose reactions to stress are shown in figure 2.

In 4 patients who continued to come to the clinic after becoming completely free of urticaria, the response to the skin tests with histamine and pilocarpine in the dilutions previously used could no longer be elicited.

Vascular Changes Following a Blow.—Since the patients saw themselves emotionally as "taking a beating," it seemed pertinent to compare the changes in their skins with those which follow a real blow. It is a matter of common experience that a blow on the skin is followed by a rise in skin temperature. It was found that the reactive hyperemia threshold dropped in both arms after a blow on only one forearm of a healthy man, and that feigning a blow produced a similar fall, though only on the threatened arm. Real trauma to the skin therefore leads, as would be expected, to those vascular changes which are associated with urticaria, and the changes can, in part at least, be elicited by merely threatening such trauma.

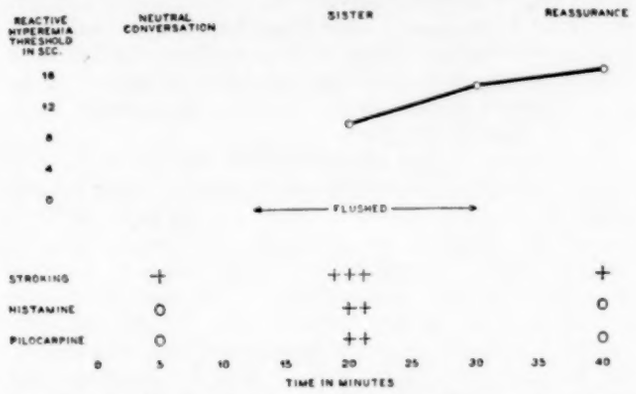

Fig. 5.—Simultaneous changes in the response of the skin to histamine, to pilocarpine and to stroking during a stressful interview with a woman patient (histamine acid phosphate 0.001 per cent and pilocarpine hydrochloride 1 per cent at only 10 microamperes for two minutes over 1 square centimeter). There was no response to isotonic sodium chloride solution applied in the same way before, during or after the period of stress.

Ten of the 30 patients showed, at one time or another, diastolic blood pressure of 100 mm. of mercury or more; 5 others had one of more diastolic pressures between 90 and 100 mg. The highest readings were usually obtained during discussions of the life situations associated with urticaria and, on the few occasions when the cutaneous vascular changes were measured concomitantly, were associated with the greatest cutaneous vasodilatation.

COMMENT

Feeling of Resentment.—In every patient who could be adequately studied there was identified one leading factor in precipitating hives. This was a feeling of intense resentment generated in situations in which the person believed that he was unjustly "taking a beating" but could neither fight nor run. Thus in every case in the series reported exacerbations and remissions of the disease showed an almost perfect correlation with a particular attitude toward life situations but correlated little or not at all with anything else. This attitude of the patient was usually quite conscious and clearly verbalized.

It is important to distinguish between resentment, the feeling so characteristic of these patients, and hostility. Resentment is "a feeling of indignant displeasure because of something regarded as a wrong or insult," while hostility is "a feeling of antagonism or enmity, implying a wish to take aggressive action." Resentment may, of course, lead to hostility, but it was significant that in these persons it usually did not.

Pattern of Attacks.—The most commonly encountered pattern was one in which urticaria first appeared in connection with resentment felt toward a person exceedingly important to the patient, such as spouse or parent, or in connection with events of major importance, such as difficulties at work. As long as this basic conflict was unresolved, many events which might otherwise have caused little disturbance were sufficient to provoke attacks. These were sometimes symbolically related to the chief problem, but often it seemed to be only a matter of the straw breaking the camel's back, a sort of summation effect.

Exceptions to the generalization that urticaria was associated only with feelings of resentment were usually found to be only apparent when the patient's attitude toward the situation was ascertained. One woman, for example, had an attack following the death of a cousin of whom she had always been fond and whom she described as much like herself. She did not feel primarily depressed, as might be inferred, but was resentful because the death was "unfair." Another had complaints chiefly referable to anxiety but had urticaria during occasional periods of resentment (fig. 3). One young man had muscle pain in the chest and began to worry about heart disease; while ruminating over this problem one night he had a recurrence of the urticaria from which he had been free for ten months. At the time the urticaria appeared he was thinking, in his own words, "This shouldn't happen to me." It is apparent that such attitudes if widely extended represent a rather paranoid formulation of life experiences.

When the patients were pressed to state what retaliatory or remedial action they had considered, the characteristic statement was, "There was nothing I could do." This view of the matter did not necessarily correspond with reality as seen by the therapist, and indeed often it seemed that several courses of action were open which were not evident to the patient.

A prominent element in some of the cases was a quite conscious indecision, a hesitation among several courses of action, which interfered with constructive handling of the problem. One woman, for instance, felt mistreated by several physicians who had given her conflicting advice; she could not make up her mind to trust herself to any one of them, and severe urticaria developed. In such persons the lesions seemed to appear only after they had given up attempts to make a decision. The effect of this, of course, is substantially the same as not seeing any possible course of action, in that both implied an inability to move off the "spot" on which they found themselves.

It should be stated that some attacks were observed in which the pertinent factors could not be determined. Also, there was one young man who insisted that lesions occasionally appeared during periods of what he called "elation" at having made progress toward solving his problems. The majority of his attacks, however, occurred like those of the other patients at times of helpless resentment. Several patients had lesions so continuously in settings of chronic resentment that identifiable exacerbations seemed sometimes to be more closely related to physical factors such as heat or mechanical trauma than to variations in their life situations.

Many of the patients had already tried eliminating from their diets various foods which they had suspected of being responsible for their diseases, and some had gone so far as to subsist entirely on water for a day or two without obtaining relief. A few stated that taking alcoholic beverages produced attacks, but they had many outbreaks without exposure to alcohol. It was surprising in view of the findings of Grant, Pearson and Comeau that none of them gave a history of significant association between muscular exercise and the appearance of lesions.

Absence of Allergic Factors.—The failure to find "allergic" factors is of particular interest, since every effort was made to obtain a truly unselected series and many of the patients were at first completely unaware that their emotional problems had anything to do with their skin trouble. However, there are several reasons why this group may not represent a truly random sample of the population of persons with chronic urticaria. First, although attempts were made to avoid it, outside physicians and members of the hospital staff probably tended to refer to the Clinic those cases in which there was some evidence that emotional factors were of importance. Second, if there are persons in whom attacks of urticaria predictably follow ingestion of certain food or chemical agents, the connection would probably be discovered either by the family physician or by the patient himself, so that he would be less likely to apply for treatment at a large diagnostic center.

It would have been interesting to investigate by the methods used in this series a person with a reliable history of urticaria following exposure to specific drugs. Unfortunately, no such person was available while the work was in progress. It seems probable that many cases in which the occurrence of urticaria predictably follows the ingestion of a particular drug are to be explained on the basis of its vasodilating power.

Relation of Attitude to Outbreaks.—Although the attitude associated with outbreaks of the disease could be defined with considerable precision, just what elements of their life experiences or their present situations predisposed these persons to take this special view of their conflicts was not so clear. An extensive experience with physical beatings did not seem to be a prerequisite for the development of urticaria later in life, and only 2 of the patients had histories suggesting that they received any unusual physical punishment from their parents. Some stated that their parents had never hit them.

In general, however, it could be said that as a group the patients had not only failed to express hostility but tended not even to feel it. (This was not invariably true, and 1 man had been rather pugnacious for much of his life, but not at times when urticaria developed.) A corollary of this was that they had for the most part adopted a rather passive attitude toward punishment from parents or other superiors. This was sometimes the result of being exposed to authoritarian and frightening parents who tolerated no expressions of aggression. One man apparently came to a conscious decision that there were more rewards in conforming and submitting to his father's wishes than in rebelling. Another was brought up by his mother and aunt to feel guilty about hostile feelings or behavior and almost all tendencies to action on his part, whether hostile or otherwise, had been frustrated by the intervention of adults. In at least 2 women the difficulty semed to be principally that they found hostility unacceptable in terms of their standards of proper behavior.

It should be emphasized that during periods of rumination, which were so frequently associated with

attacks of urticaria, the patients did not have hostile, aggressive fantasies. It seems probable that such fantasies are incompatible with the type of vascular behavior which leads to urticaria. One man stated clearly that after he had ceased to have attacks after quarrels with his superior he had aggressive feelings which might or might not be expressed in speech or action, but that while he was still having urticaria he had not had such fantasies.

The passivity with respect to hostile actions of others was not necessarily joined to a generally passive attitude in life. Some of the patients manifested considerable energy and initiative in their jobs, for instance; others were generally fearful and unassertive. Difficulty in dealing with situations which revolve around the expression of hostility is, of course, common in many different disorders. The feature peculiar to patients with urticaria is the failure to generate hostile feelings to any significant extent even though circumstances may seem to call for them. They are preoccupied with what is being done to them rather than with what they are going to do.

Influence of Dilatation.—All the evidence presented with respect to the skin changes indicates that the essential difficulty is an increased tendency of both arterioles and minute vessels to dilatation. In other words, the vessels behave as they would have if the person had actually been receiving blows. This dilating tendency was exemplified in the increased sensitivity of the skin to local histamine and pilocarpine and in dermographism. Generalized whealing after the application of vasodilating stimuli, such as heat or pilocarpine, may be looked on as merely an exaggeration of the dilatation which such agents produce in anyone. Previous interpretations of these phenomena have been complicated by the assumption that the explanation of wheal formation must include some factor other than simply the dilatation itself. Thus Grant, Pearson and Comeau [1b] assumed that acetylcholine liberated at vasomotor nerve endings in some way brought about the release of histamine, so that the complete urticarial lesion appeared.

It is much simpler to suppose that urticaria is nothing more than the end result of intense vasodilatation and that no additional factor is necessary. The contrary view has apparently been adopted because of Lewis' conclusion that a diffusible substance in the skin, probably histamine, is responsible for the triple response and that it must have some direct effect on the capillary wall to account for increased permeability. The argument in support of the latter point, however, does not in fact rule out the simpler assumption previously mentioned, that permeability increases as the capillary dilates. It is therefore not necessary to assume that the local effect of histamine is achieved through any other mechanism than vasodilatation or that clinical urticaria requires the participation of histamine or a similar substance.

This does not conflict with the idea that there is released at the site of trauma to the skin a diffusible chemical compound, which may be histamine or something closely related, responsible for the local dilatation. Mild local trauma, possibly because it provoked release of such an H-substance, seemed to be a factor of considerable importance in determining the exact location of lesions by locally increasing the general tendency to vasodilatation. Since it is practically impossible to shield the skin from any stimulation whatever, it is even conceivable that lesions appear only at sites where there has been some slight trauma. Some of the lesions which appeared during interviews, however, were at places where previous stimulation had not been observed. The essential point is that the susceptibility of the skin to such stimulation varies.

Flushing.—There are, of course, circumstances other than those arousing resentment in which cutaneous vasodilatation occurs and in which urticaria might therefore be expected. One of the commonest is a social situation inducing what is usually called "embarrassment." Although this feeling seemed to be present in association with a small number of the episodes of urticaria which the patients reported, it was not unequivocally shown to be a major factor in any of the attacks, probably because it tends to be relatively short-lived. Casual observations of 1 woman who was not a patient revealed one or two small urticarial lesions on the face at such times. (Questioning of persons who blush easily when embarrassed often elicits information indicating that there is a large admixture of resentment in their feeling.) In another young woman the pleasant anticipation of social events, particularly during heightened attention to the face while applying cosmetics, was often associated with the appearance of an urticarial lesion.

The reason, then, that the patients in this study had urticaria is that they responded to many of their life situations by a generalized cutaneous vasodilatation, involving both arterioles and minute vessels, as the foregoing experiments demonstrate. This appeared first as flushing, and if it was sufficiently intense and prolonged urticaria appeared. At the time of the attacks of the disease the patients saw themselves as unjustly receiving punishment and became resentful. The entire process as it developed in them can be regarded as an intensification of the familiar skin reddening of anger. Weiss [8] also concluded that urticaria was the result of extreme flushing, though his evidence was limited. The tendency already noted herein to an elevation of arterial blood pressure in response to the traumatizing situation is probably also a factor in increasing transudation of fluid.

In this connection Schroeder and Goldman [9] recently discussed a group of patients with arterial hypertension who show cutaneous flushing. The problem of itching with urticaria will be discussed elsewhere.[10] However, when scratching occurs for whatever reason it will augment the tendency to form lesions.

SUMMARY AND CONCLUSIONS

1. Thirty unselected cases of chronic urticaria were investigated to determine the relationship between stressful life situations and the cutaneous processes responsible for the disease.

2. Attacks of urticaria were highly correlated with emotional disturbances of a particular kind. No relation was discovered between exposure to allergens and attacks of the disease.

3. Traumatic life situations responsible for lesions were almost exclusively those in which the patient felt resentment because he saw himself as the victim of unjust treatment about which he could do nothing.

8. Weiss, S.: The Interaction Between Emotional States and the Cardiovascular System in Health and Disease, in Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman, by His Pupils, Friends and Colleagues, New York, International Press, 1932, vol. 3, pp. 1181-1198.

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10. Graham, D. T.; Goodell, H., and Wolff, H. G.: To be published.

4. Experimental study of cutaneous vascular reactions indicated that the disease was the result of extreme dilatation of both arterioles and minute vessels in the skin that occurred as part of the patient's reactions to such situations. These are the same changes as those which occur after actual trauma to the skin.

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MENINGITIS DUE TO SIMULTANEOUS DOUBLE INFECTIONS IN CHILDREN

EDWIN B. VADEN, M.D.
E. CLARENCE RICE, M.D.
and
VERA STADNICHENKO, M.S.
Washington, D. C.

Few cases of meningitis due to a simultaneous double infection, with isolation of two or more organisms from the initial examination of the cerebrospinal fluid, have been reported. We have found references to only 13 cases in the literature, although reports of mixed meningitis due to a secondary organism are frequently encountered.

In the thirty month period from January 1947 to July 1949, 10 patients with simultaneous double infection of the meninges were observed at the Children's Hospital. These 10 patients represent 8.0 per cent of the total number (124) of patients who were treated for purulent meningitis in this period. We are reporting on these cases because of their apparent rarity and because we believe that many unrecognized and unreported cases of simultaneous mixed meningitis occur. Perhaps an increased awareness of the high incidence of double meningitis will produce an increase in the number of such patients discovered in the future.

In 9 of the 10 patients, Hemophilus influenzae (type B in 8 and type A in 1) was one of the offending organisms. One patient had meningitis due to Diplococcus pneumoniae and Escherichia coli. The influenza bacillus was associated with Neisseria intracellularis in 4 cases, streptococcus in 3 cases and D. pneumoniae in 2 cases. The various combinations of organisms are shown in table 1.

The first patient observed with a simultaneous infection, a 5 year old white boy, was admitted in February 1947 with a history of cold and fever of about twenty-four hours' duration. A generalized petechial rash had developed just prior to admission. The boy presented the classic picture of meningitis. The spinal fluid contained 7,500 leukocytes per cubic millimeter. A stained smear showed a gram-negative diplococcus. The same organism was found on examination of a petechial smear, and a diagnosis of meningococcic meningitis was made. By the second hospital day, however, colonies of both N. intracellularis and H. influenzae were found on culture of the initially obtained cerebrospinal fluid. The latter organism was subsequently typed as H. influenzae, type B. The presence of these two organisms in the spinal fluid was of especial interest to one of us (V. S.), and in all subsequent cases of meningitis the patients were carefully examined for double infection. Frequently one of the organisms has shown such poor growth that subsequent isolation and identification has been made with considerable difficulty.

From the Departments of Pathology and Medicine, Children's Hospital, Washington.

INCIDENCE

This series is made up of 5 boys and 5 girls. Seven of the patients were white; 3 were Negro. The age incidence is of interest (table 2). The youngest patient was 11 weeks of age and the oldest 5 years. Six of the patients were under 18 months of age, 5 of these being under 1 year. The remaining 4 patients were between the ages of 4 and 6 years.

The usual clinical course did not differ from that in other cases of purulent meningitis. The onset was preceded by an infection of the upper part of the respiratory tract with fever, irritability and lethargy for twenty-four to forty-eight hours. Two of the patients exhibited generalized petechiae on admission, and the petechial smears were positive for gram-negative intracellular diplococci. In 4 patients there was a history of vomiting and in 3, all less than 1 year of age, a history of generalized convulsions. In all patients the diagnosis of meningitis was suggestive enough at admission to warrant the performance of a lumbar puncture. The presence of a bulging fontanel was a prominent sign in the younger infants.

The temperature at admission varied from 99.4 F. to 104.4 F. The duration of the fever, from time of onset, varied from six to seventeen days, and the period of hospitalization ranged from eleven to thirty-three days. It is interesting to note that in the more recent cases patients have been hospitalized for approximately one-half the time of patients in the earlier cases. This is probably due to earlier recognition of the mixed character of the infection, with initiation of appropriate therapy, and especially the use of larger doses of penicillin.

TABLE 1.—*Combinations of Organisms*

Organisms	No. of Cases
H. influenzae and N. intracellularis	4
H. influenzae and Streptococcus	3
H. influenzae and D. pneumoniae	2
D. pneumoniae and Esch. coli	1
Total	10

TABLE 2.—*Age Distribution*

Age	No. of Patients
1 to 6 months	3
6 to 12 months	2
1 to 2 years	1
2 to 4 years	0
4 to 6 years	4

LABORATORY DATA

Table 3 shows the conditions revealed by the examination of the cerebrospinal fluid at admission. The fluid appeared grossly cloudy in each instance. The leukocyte count varied from 350 to 14,000 per cubic millimeter, and the polymorphonuclear cells always predominated. The protein level was elevated, ranging from 50 to 500 mg. per hundred cubic centimeters and the amount of sugar was either reduced or absent. The stained smear was reported as showing two organisms in most cases, and two organisms were grown from the initial spinal fluid culture in every case except 1. In this patient (A. S.) there was a gram-negative intracellular diplococcus in the petechial smear, and the admission blood culture was reported positive for N. intracellularis. The spinal fluid smear showed a gram-negative diplococcus and a gram-negative bacillus, but culture of the same fluid grew only H. influenzae, type B. Despite the failure to isolate

N. intracellularis from the spinal fluid culture, the presence of the N. intracellularis bacteremia is confirmatory evidence of the presence of a double infection of the meninges.

Blood cultures were taken at admission on all patients. In 3 patients there was a mixed bacteremia, the organisms being identical to those recovered from the spinal fluid. Three other patients had positive blood cultures with only one of the offending organisms being isolated. In the remaining 4 patients the blood cultures revealed no growth. The hemogram revealed leukocytosis (10,000 to 20,000 leukocytes per cubic millimeter) in all patients. A moderate degree of anemia was not uncommon. As previously mentioned, the petechial smears were positive for gram-negative diplococci in 2 patients.

TREATMENT

No attempt will be made to discuss the treatment of meningitis in this paper. In addition to parenteral fluids and whole blood all the patients received sulfadiazine and penicillin. Streptomycin was employed in most cases in which H. influenzae was present. Interestingly enough, in 2 patients (A. S. and J. M.) with a mixed meningococcic and influenzal meningitis, the latter organism was not positively identified for several days. In the meantime the patients were treated for meningococcic meningitis with sulfadiazine and penicillin. They showed such dramatic improvement with these two drugs that streptomycin was never utilized. The patients completely recovered.

The dosage of sulfadiazine was calculated at 0.3 Gm. per kilogram of body weight each twenty-four hours. It was given subcutaneously for the first few days of therapy or until the patient could take the drug by mouth. The levels of sulfadiazine in the blood were utilized as a guide in determining the amount of the drug given.

The dosage of penicillin varied greatly among the patients. In the earlier cases patients received approximately 800,000 units daily, whereas in the more recent cases patients have been given up to 8,000,000 units daily. Penicillin was injected intramuscularly in divided doses, at two or three hour intervals. Penicillin was administered intrathecally in 3 cases.

Streptomycin, in divided intramuscular doses totaling approximately 1 Gm. per day, was utilized in 7 cases. Intrathecal instillation of the drug was used in 4 cases. The drug was continued for a total of seven to eleven days, depending on the rapidity with which the spinal fluid returned to normal.

Type specific H. influenzae antiserum (type B) was used in only 2 patients, 1 of whom subsequently was found to have a type A instead of type B organism.

MORBIDITY

No fatalities occurred among these patients. Seven were discharged with no apparent damage to the central nervous system. The 3 remaining patients had some evidence of neurologic involvement at the time of discharge. One patient had hemiparesis on the right side, although she could stand and walk several months after the onset of the disease. Another patient, examined by a neurologist on the eighteenth hospital day, showed spasticity of the extremities on irritation or awakening. A third child showed evidence of a subarachnoid block with generalized hypertonicity and weakness on the left side of the face at the time of discharge.

TABLE 3.—*Results of Cerebrospinal Fluid Examination and Blood Cultures Made at Admission*

			Cerebrospinal Fluid							
Patient	Age	Sex	Appearance	Leukocytes (per Cu. mm.)	Polymorphonuclear Cells (per 100 Cc.)	Protein (Mg./100 Cc.)	Sugar (Mg./100 Cc.)	Smear*	Culture	Blood Culture
J. M.	5 years	M	Cloudy	7,500	98	110	35	Gm. neg. diplococci	N. intracellularis H. influenzae	No growth
G. B.	3 mo.	M	Cloudy	350	86	100	0-10	Gm. neg. bacilli	Str. viridans H. influenzae	No growth
A. S.	4 years	F	Cloudy	10,850	98	500	45	Gm. neg. diplococci Gm. neg. bacilli	H. influenzae	N. intracellularis
E. T.	9 mo.	F	Cloudy	375	63	200	0	Gm. pos. diplococci Gm. neg. bacilli	Esch. coli D. pneumoniae 2	Esch. coli
H. D.	3 mo.	M	Cloudy	7,900	72	150	0-10	Gm. neg. bacilli	H. influenzae Nonhemolytic streptococci	No growth
S. Q.	8 mo.	F	Cloudy	3,325	89	400	0	Gm. neg. bacilli Gm. neg. diplococci	H. influenzae N. intracellularis	H. influenzae N. intracellularis
D. G.	3 mo.	M	Turbid	520	82	100	5	Gm. pos. diplococci Gm. neg. bacilli	D. pneumoniae H. influenzae	D. pneumoniae
M. P.	1 year, 4 mo.	M	Cloudy	2,000	61	80	40	Gm. neg. bacilli Gm. pos. cocci	H. influenzae Nonhemolytic streptococci	No growth
K. G.	4 years	F	Turbid	6,900	90	300	0	Gm. neg. bacilli Gm. pos. diplococci	H. influenzae D. pneumoniae 14	H. influenzae
J. T.	5 years	F	Cloudy	14,000	92	200	20	Gm. neg. bacilli Gm. neg. diplococci	H. influenzae N. intracellularis	H. influenzae N. intracellularis

* Gm. neg. = gram-negative, gm. pos. = gram-positive.

LITERATURE

The literature on simultaneous double infection of the meninges is scanty and consists mainly of scattered case reports. Neal [1] reported the largest number of cases. She reviewed 1,535 cases of meningitis which occurred in New York City over a period of fourteen years and noted only 6 cases (0.32 per cent) of "mixed infection," all occurring in children. No details of the individual cases were given, and we must assume that these represent true double infections rather than secondary infections. Ashmun [2] reported 5 patients,

1. Neal, J. B.: Meningitis: Distribution According to Age and Etiology, J. A. M. A. **82**: 1429 (May 3) 1924.
2. Ashmun, S. H.: Pneumococcic Meningitis Combined with Streptococcus and Diplococcus Catarrhalis, Ohio State M. J. **29**: 243, 1933.

all children, with mixed infection, but in only 4 of these was more than one organism grown from the initial spinal fluid culture. In each of his patients D. pneumoniae and streptococcus were found, and in 2 of the patients Neisseria catarrhalis was also present.

Gaffney [3] observed a 10 month old boy who had double meningitis caused by D. pneumoniae (type 8) and H. influenzae. Cunningham [4] reported a case of double meningitis (N. intracellularis and hemolytic streptococci) secondary to otitis. The double character of the infection was recognized late in the disease, at which time reexamination of the original blood plate revealed a few colonies of previously unrecognized streptococci associated with a good growth of N. intracellularis.

Mouriquand and Sédallion [5] reported 2 cases of mixed infection in infants. The first case represents a secondary infection, since the two organisms (N. intracellularis and D. pneumoniae) were cultured from the fluid obtained at the third lumbar puncture. The two previous spinal fluid cultures had grown the N. intracellularis only. Their second case represents a true simultaneous double infection, with N. intracellularis and D. pneumoniae being isolated on smear and culture at the first lumbar puncture. This patient, a 2 month old boy, died after six weeks.

Fiddes [6] reported the case of a 14 month old boy with a mixed infection of the meninges due to the tubercle bacillus and N. intracellularis. He stated that it " . . . is rare to find two different causative organisms in a case of meningitis and of extreme rarity when one of these organisms is the tubercle bacillus." We have found that in over one-half the reported cases of simultaneous double infection the tubercle bacillus is one of the offending organisms. We prefer to consider these cases in which the tubercle bacillus is present as secondary mixed infection, inasmuch as we believe that the meninges are invaded primarily by Mycobacterium tuberculosis and secondarily by the pyogenic organism. Such a sequence of events is illustrated excellently by the postmortem observations in Fiddes' patient. He found a primary tuberculous focus in the lung which was fibrotic and presumably acquired some months before death. The onset of the tuberculous meningitis was estimated to be about six weeks before admission, when a change in the patient was first noticed. The finding of a tuberculoma in the brain substance and miliary tubercles in the brain surface was evidence of the long-standing intracranial involvement. Fiddes suggested that the child was a probable carrier of meningococci in his throat and that the organisms presumably became sufficiently virulent to cause meningitis just one week before admission.

Several additional cases [7] have been reported in which the tubercle bacillus has been associated with the meningococcus. Other organisms which have been associated with the tubercle bacillus are Klebsiella pneumoniae (Friedlander's bacillus),[8] Diplococcus crassus [9] and diplococcus closely allied to the Gaffkya tetragena.[10]

3. Gaffney, J. C.: Mixed Infection of Meninges with H. Influenzae and the Pneumococcus, Brit. M. J. **1**: 346, 1940.

4. Cunningham, A. A.: Mixed Meningococcal and Streptococcal Meningitis, Lancet **1**: 198, 1937.

5. Mouriquand, G., and Sédallion, P.: Méningites à méningocoques et à pneumocoques associés, Lyon méd. **138**: 664, 1926.

6. Fiddes, J.: Combined Forms of Meningitis: Mixed Infection of the Meninges by the Tubercle Bacillus and Meningococcus, Arch. Dis. Childhood **16**: 140, 1941.

7. Déléarde and Petit, G.: Sur un cas de méningite polymicrobienne à bacilles de Koch et à diplocoques, Echo méd. nord **10**: 201, 1906. Armand-Delille, P., and Berthaux, R.: Un cas de méningite avec association de bacilles de Koch et de meningocoques de Weichselbaum, Ann. Med. Chir. Inf. **11**: 400, 1907. Mikulowski, W.: Infection méningée mixte à diplocoque de Weichselbaum et à bacille de Koch, Arch. méd. d. enf. **34**: 671, 1931. Lemieux, R.; Morin, E., and Nadeau, H.: Infection méningée tuberculeuse et méningococcique, Laval méd. **9**: 295, 1944.

8. von Moritz, D.: Mischinfektion der Hirnhäute mit dem Koch- und dem Friedländerschen Pneumo-Bazillus, Arch. f. Kinderh. **109**: 21, 1936.

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SUMMARY AND CONCLUSIONS

1. Ten cases of meningitis due to a simultaneous double infection in children have been reported. This represents 8.0 per cent of all cases of purulent meningitis at the Children's Hospital in a thirty month period.

2. In 9 of the patients Hemophilus influenzae was one of the offending organisms. The associated organisms, in order of frequency, were Neisseria intracellularis (4 cases), streptococcus (3 cases) and Diplococcus pneumoniae (2 cases). The meningitis in 1 patient was due to D. pneumoniae and Escherichia coli.

3. All patients were 5 years of age or under, 5 being less than 1 year of age.

4. In all patients except 1 both organisms were isolated from culture of the spinal fluid taken at the initial examination. In 1 patient two organisms were seen on the original spinal fluid smear, but only one was cultured. However the other organism (N. intracellularis) was found on both blood culture and examination of petechial smears.

5. All the patients were treated with sulfadiazine and penicillin, and 7 also received streptomycin. The drugs were administered in accepted dosages for the period in which the patients were seen. Massive doses of intramuscularly administered penicillin have been used in the more recent cases, and this appears to have shortened the course of the disease. There were no fatalities among these patients.

6. Only 13 cases of simultaneous double meningitis have been found in a review of the literature. Doubtless other cases have been observed and many cases have gone unrecognized.

7. Because of the high incidence of double infection seen in this hospital we suggest that every child with purulent meningitis be treated for a mixed infection until bacteriologic studies are completed.

Purveyal of Medical Service.—A physician should not dispose of his professional attainments or services to any hospital, lay body, organization, group or individual, by whatever name called, or however organized, under terms or conditions which permit exploitation of the services of the physician for the financial profit of the agency concerned. Such a procedure is beneath the dignity of professional practice and is harmful alike to the profession of medicine and the welfare of the people.

Physicians as Citizens.—Physicians, as good citizens, possessed of special training, should advise concerning the health of the community wherein they dwell. They should bear their part in enforcing the laws of the community and in sustaining the institutions that advance the interests of humanity. They should cooperate especially with the proper authorities in the administration of sanitary laws and regulations.

Pharmacists.—Physicians should recognize and promote the practice of pharmacy as a profession and should recognize the cooperation of the pharmacist in education of the public concerning the practice of ethical and scientific medicine.

From the PRINCIPLES OF MEDICAL ETHICS of the American Medical Association.

CHLORAMPHENICOL IN THE TREATMENT OF HEMOPHILUS INFLUENZAE MENINGITIS

GEORGE W. PRATHER, M.D.
and
MARGARET H. D. SMITH, M.D.
New Orleans

Whereas the mortality from meningitis due to Hemophilus influenzae has fallen remarkably during the past decade, several recent reports bear witness that there is still leeway for improvement in treatment of this disease. In well equipped hospitals, 63 to 90 per cent of patients with this type of meningitis survive [1]; however, many survivors show evidence of permanent brain damage, so that odds for complete recovery vary from 44 to 73 per cent.[2] The outlook under less than the most favorable conditions is undoubtedly poorer. What seems to be needed are (1) means of shortening the period of active infection, i. e., even more effective therapeutic agents, and (2) a way to lessen damage due to increased intracranial pressure. As to consideration of the first need, the present paper reports on the efficacy of chloramphenicol (chloromycetin®) in treatment of meningitis due to H. influenzae.

Two other recent antibiotics which have gained favor in management of this disease are streptomycin [3] and aureomycin.[4] In the case of streptomycin the frequent emergence of resistant organisms and the necessity of intrathecal administration, as well as the toxic effects on the eighth nerve, constitute serious objections to its use. When aureomycin is employed, the bacteriologic response is sometimes slow; in some reports cultures of spinal fluid remained positive for as long as four days.[4b]

Chloramphenicol has been found to be very active against Hemophilus pertussis and H. influenzae in vitro.[5] It was reported in April 1949 that chloramphenicol readily passes into the spinal fluid, where it reaches concentrations ranging from 30 to 50 per cent of that in the blood.[6] These facts, together with our favorable impression of the drug in the management of some infections due to Salmonella, led us to try it in a series of 15 consecutive unselected patients with H. influenzae type B meningitis admitted between May 1949 and March 1950.

CLINICAL FEATURES

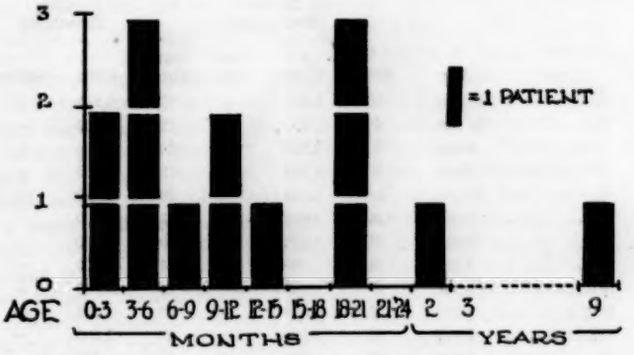
Age Incidence.—The youngest patient in the group was 6 weeks of age and the oldest 9 years. It is worth emphasizing that 8 of these patients were less than 1 year of age, i. e., in an age group in which prognosis for recovery from meningitis is notoriously poor.

Clinical Picture on Admission and Laboratory Findings.—Most of our patients were seriously ill on admission. Many came from outlying areas and had traveled long distances; none could be considered on the basis of their clinical appearance as "good risks."

Of the 15 patients, 8 were irregularly treated with one of the sulfonamides or antibiotics prior to treatment with chloramphenicol. In 3 of these patients the spinal fluid cultures were negative on admission. They are included here because H. influenzae type B was recovered from the spinal fluid on admission.

CASE 8.—A dangerously sick Negro male infant of 7 months had received 85 mg. of aureomycin every four hours and a total of 800,000 units of penicillin five days before meningitis was suspected; at admission, smears and Neufeld's reactions were positive for H. influenzae, though no positive culture was secured.

CASE 9.—A white female infant of 6 weeks had received one dose each of penicillin, sulfadiazine and chloramphenicol during twenty-four hours prior to admission for symptoms of respiratory disease before meningitis was suspected. When the patient was admitted, however, smears and Neufeld's reactions were positive for H. influenzae type B, but cultures remained negative.



Age of patients treated with chloramphenicol. The vertical row of figures on the left shows the number of patients.

CASE 10.—A 9 year old Negro girl had been sick for six days prior to admission and had received a single dose of 200,000 units of penicillin intravenously twelve hours before admission. On admission, organisms were identified on direct examination of the spinal fluid, though cultures remained negative.

Specimens of spinal fluid drawn at the time of admission showed usual variations in cell count and sugar content; in all but 3 cases the level of spinal fluid sugar was under 22 mg. per hundred cubic centimeters. H. influenzae was identified by direct smear and Neufeld's reaction in all 15 patients and was later confirmed by culture in 12 of these.

PLAN OF TREATMENT

The dosage schedule adopted for chloramphenicol was the one we had found satisfactory in the treatment of typhoid. We planned to give the patient on admission 75 to 100 mg. per kilogram of body weight of the drug orally—by gavage if necessary; this was followed by 250 mg. every eight hours, regardless of body weight. For various reasons, the initial dose actually received varied between 42 and 111 mg. per kilogram; it was administered orally in all but 1 patient, whose intractable vomiting made rectal administration necessary. In

From the Department of Pediatrics, Tulane Medical School and the Charity Hospital of Louisiana at New Orleans.

The chloramphenicol used in the early part of this study was supplied by Dr. Eugene Payne of Parke, Davis & Company, Detroit.

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this patient, a cleansing enema preceded the first dose of the drug; the capsules were pierced before insertion, the buttocks were taped together and diapers were carefully checked to ascertain that no capsules were extruded. Treatment with the drug was continued for five to fourteen days, depending on the patient's course.

Because this agent was new and its efficacy in influenzal meningitis uncertain, it seemed wise at first to give type-specific antibody in addition. The first patient received 175 mg. of rabbit antibody nitrogen, the second, 100 mg. and the third and fourth, 150 mg. each. Except as previously described, sulfonamides and other antibiotics were not given. Two patients were later treated with sulfonamides and penicillin when secondary infections developed. No toxic manifestations attributable to the drug were observed.

COURSE OF THE DISEASE AND RESULTS

All 15 patients recovered. Not all, however, convalesced without complications. In early convalescence, 3 patients vomited persistently and had a bulging fontanelle and convulsions. These symptoms suggested the presence of a subdural effusion of fluid,[7] confirmed in each by subdural tap. In a fourth patient an asymptomatic subdural effusion was discovered by means of a "routine" subdural tap.[7b] All 4 of these patients were completely well at discharge. One patient, in whom fever, dyspnea and anorexia persisted after the spinal fluid was normal, had atelectasis and pneumonia of the upper lobe of the right lung, for which no satisfactory bacterial cause could be established. These symptoms subsided after therapy with sulfadiazine, penicillin, streptomycin and anti-influenzae type B rabbit antibody. Another child, who also remained febrile and dyspneic after clearing of the spinal fluid, had clinical and roentgenographic evidence of diffuse pneumonitis, which cleared promptly after penicillin was given. Two patients had transient arm and leg muscle weakness.

Early Changes in Cerebrospinal Fluid

			Before Treatment*			After Treatment†	
Case	Age	Sex	Cells	Culture	Interval, Hours	Cells	Smear
1.....	30 mo.	M	8,400	+	16	5,240	+
2.....	30 mo.	F	800	+	12	400	—
3.....	2 mo.	F	2,800	+	26	5,000	+
4.....	5 mo.	F	2,800	+	15	6,000	+
5.....	12 mo.	M	1,350	+	20	6,120	+
6.....	6 mo.	M	1,200	+	32	2,300	—
7.....	20 mo.	M	1,400	+	29	1,000	—
8‡.....	7 mo.	M	1,100	—	24	650	—
9‡.....	6 wk.	F	9,000	—	24	12,000	+
10‡.....	9 yr.	F	3,820	—	36	214	—
11.....	2 yr.	F	1,800	+	23	1,000	—
12.....	6 mo.	M	270	+	24	750	—
13.....	14 mo.	M	550	+	10	2,260	—
14.....	8 mo.	M	1,100	+	14	900	—
15.....	11 mo.	M	1,020	+	22	610	—

* All smear and Neufeld reactions were positive before treatment.
† All cultures were negative after treatment.
‡ See text for brief descriptions of other therapy.

All these infants were hospitalized for two weeks or more. At the time of discharge all were asymptomatic with the exception of 1 child, who, although bright and playful, still displayed moderate weakness of one arm and leg. This was slowly improving when he was discharged on the twenty-first day. When seen one month later, he had entirely recovered.

As to results observed in the laboratory, the striking feature was the rapidity with which cultures of spinal fluid became negative after the start of chloramphenicol therapy. Even in patients admitted during the night—with the spinal fluid teeming with organisms—a new specimen of spinal fluid planted the next morning yielded no growth. When initial spinal fluid specimens contained many organisms, a few could still be found on smear the next day, but they failed to grow. In 1 patient a single dose of chloramphenicol (presumably 250 mg.) given twenty-four hours before admission had apparently sterilized the spinal fluid, though a few organisms of typical morphology were seen on smear, and these were proved to be H. influenzae type B by direct Neufeld reaction. This failure to recover the organism on subsequent cultures is in contrast to our experience and that of others using other therapeutic regimens.

COMMENT

The disease in these patients was of average severity, so that recovery in 15 consecutive unselected cases is most gratifying. We attribute these good results to the efficacy of chloramphenicol and would like to point out that this form of therapy is particularly satisfactory because the drug can be given orally without disturbing the patient for intrathecal or intramuscular injections and because it is possible to eliminate serum reactions which are apt to be most severe in extremely sick patients.[8]

Optimal dosage schedules remain to be worked out. The case of a severely ill 6 week old infant, whose spinal fluid had apparently been sterilized by one dose of chloramphenicol given by mouth twenty-four hours prior to admission, suggests that the efficacy of chloramphenicol in H. influenzae meningitis approaches that of sulfonamides in meningococcic meningitis.

SUMMARY AND CONCLUSION

1. Fifteen consecutive patients, 8 of them under 1 year of age, had meningitis bacteriologically proved to be due to Hemophilus influenzae type B and were treated with chloramphenicol; all recovered.

2. In every case spinal fluid was sterile on the second lumbar puncture, performed within an average interval of twenty-one hours.

3. No toxic effects attributable to the drug were observed.

4. Although an optimal dosage regimen has yet to be worked out, a good starting point suggested by these observations would be 50 to 100 mg. per kilogram of body weight by mouth or by stomach tube on admission, followed by 250 mg. every eight hours thereafter for five or more days, regardless of weight.

5. We believe this method of treating meningitis due to H. influenzae type B to be more satisfactory than any other we have had an opportunity to use.

7. (*a*) McKay, R. J., Jr.; Morissette, R. A.; Ingraham, F. D., and Matson, D. D.: Collections of Subdural Fluid Complicating Meningitis Due to Haemophilus Influenzae (type B): A Preliminary Report, New England J. Med. **242**: 20, 1950. (*b*) Smith, M. H. D.; Dormont, R. E., and Prather, G. W.: Subdural Effusions of Fluid Complicating Meningitis, to be published.

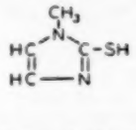
8. Smith, N. H. D.; Wilson, P. E., and Hodes, H. L.: Treatment of Influenzal Meningitis, J. A. M. A. **130**: 331 (Feb. 9) 1946.

TREATMENT OF HYPERTHYROIDISM WITH 1-METHYL-2-MERCAPTOIMIDAZOLE

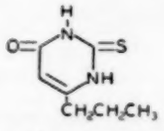
WILLIAM S. REVENO, M.D.
and
HERBERT ROSENBAUM, M.D.
Detroit

We have used a new antithyroid drug, 1-methyl-2-mercaptoimidazole (tapazol), in the treatment of 18 patients with hyperthyroidism during a six month period and have found it fully as efficient as thiouracil and propylthiouracil in this condition. Toxic reactions were not observed.

The new compound is one of the imidazoles and differs from the well known antithyroid drugs in that it has a five-membered rather than a six-membered ring. (See the accompanying structural formulas.)



1-Methyl-2-Mercaptoimidazole



6-Propyl-2-Thiouracil

Its powerful antithyroid activity was noted by Stanley and Astwood [1] when they were testing a number of similar compounds by the radioactive iodine technic.[2] A pronounced effect on iodine accumulation in the thyroid was noted with as little as 0.5 mg. of the compound, and 5.0 mg. completely inhibited the uptake of iodine for nearly twenty-four hours.

Comparative studies place the action of the drug above that of thiouracil, methylthiouracil, propylthiouracil and 2-mercaptoimidazole and rate its potency at a hundred times that of thiouracil. In actual clinical trial the drug appears to be twenty to fifty times as powerful as thiouracil and acts best when administered in doses of 2 to 5 mg. every eight hours.[3]

In the group of patients with hyperthyroidism under our care, 6 had not had treatment previously, 10 had been well controlled on maintenance doses of propylthiouracil and 2 were in relapse one year and six months, respectively, after remission had been induced with propylthiouracil. Three of the first 6 had toxic diffuse goiter. All were females whose ages were 14, 12 and 27 years. The other 3 had toxic adenoma; 2 were men aged 50 and 61 and 1 a woman aged 75. Seven of the 10 patients transferred from propylthiouracil were women ranging in age from 36 to 82 and 3 were men 19, 44 and 60 years of age. The 2 patients in relapse were men aged 45 and 68 years.

REPORT OF CASES

Records of the patients with toxic diffuse goiter and 1 of the 3 with toxic adenoma are summarized in the following case reports:

CASE 1.—M. A., a school girl aged 14, had had nervousness, excess sweating, emotional instability, fatigue, increased appetite, tachycardia, gradually enlarging goiter and exophthalmos during a period of two months. The basal metabolic rate was +30 per cent, the weight 94 pounds (42.6 Kg.) and the white blood cell count 8,650 with 48 per cent polymorphonuclear cells. The thyroid gland was diffusely enlarged, and a systolic bruit was heard over both lobes. Exophthalmos, conjunctival congestion and lidlag were present. Fine manual tremor was observed, and the palms were moist and warm.

Two milligrams of 1-methyl-2-mercaptoimidazole was given every eight hours and a mild sedative at bedtime. The patient was allowed to continue at school. At the end of two weeks the weight had increased by 4 pounds (1.8 Kg.), the basal metabolic rate was +11 per cent and there was evident general improvement. At the end of sixty days' treatment the basal metabolic rate was —2 per cent, the weight had increased a total of 10 pounds (5 Kg.), most of the symptoms had disappeared, the exophthalmos had diminished, the thyroid was smaller and firmer, and the bruit had disappeared. The white blood cell count was not appreciably changed.

Treatment with the same amount of drug was continued for the next ten weeks, during which there was continued improvement and the basal metabolic rate dropped to —12 per cent. She has continued to receive a maintenance dose of 5 mg. of the drug daily for seven weeks; her weight has not changed; the exophthalmos is diminishing, and the thyroid is becoming smaller. The basal metabolic rate is —9 per cent and the white blood cell count 8,400 with 55 per cent polymorphonuclear cells.

CASE 2.—S. B., a school girl aged 12, with practically the same symptoms as in case 1, but of ten months' duration, weighed 69 pounds (31.3 Kg.), had an initial basal metabolic rate of +22 per cent and a white cell count of 9,350 with 61 per cent polymorphonuclear leukocytes.

She, too, was given 2 mg. of 1-methyl-2-mercaptoimidazole every eight hours and showed improvement in symptoms and a weight gain of 3 pounds (1.3 Kg.) in two weeks. After sixty days' treatment most of the subjective signs had improved, the exophthalmos and goiter were receding, and she had gained 6½ pounds (3 Kg.). The blood picture was unaltered. The basal metabolic rate, however, was +15 per cent, and the drug dosage was increased to 2 mg. every six hours for the next ten weeks. Improvement continued, the weight increased another 10 pounds and there was no change in the blood picture, but the basal metabolic rates on various occasions were +22, +26, +14, +30, +9 and +18 per cent. Dosage was again increased to 5 mg. every twelve hours for two weeks, then every eight hours for four more weeks. The weight increased another 2 pounds (0.9 Kg.), the eye signs, sweating and tremor subsided and the thyroid was smaller, but the basal metabolic rates were +31 and +20 per cent on two occasions. The girl remained in the euthyroid state while receiving a maintenance dose of 5 mg. of the drug daily for four weeks. The irregular behavior of the basal metabolic determinations was due to emotional disturbance.

CASE 3.—G. M., a woman aged 27, a housewife, had had palpitation, heat intolerance, nervousness, increased bulging of the eyes and enlargement of the neck and voracious appetite without weight change for about a year. The thyroid showed diffuse enlargement with systolic bruit, and there was pronounced exophthalmos and lidlag. The palms were warm and moist and showed a fine tremor; the pulse rate was 144 and the blood pressure 150 systolic and 80 diastolic. The basal metabolic rate was +73 per cent, the white blood cell count was 7,650 with 66 per cent polymorphonuclear leukocytes, and the blood cholesterol level was 167 mg. per hundred cubic centimeters. The weight was 117 pounds (53.1 Kg.).

Five milligrams of 1-methyl-2-mercaptoimidazole was given to the patient every twelve hours, and subjective improvement was noted at the end of two weeks. Although there was no change in weight, the basal metabolic rate was +46 per cent. After another four weeks there was further subjective improvement, the weight had increased 4 pounds, the pulse rate was 94, the blood pressure 130 systolic and 80 diastolic and the basal metabolic rate +34 per cent. The thyroid was smaller, and the bruit had disappeared. There was no change in the exophthalmos. The white blood cell count was 5,000 with 57 per cent polymorphonuclear cells. At the end of eight weeks all symptoms had subsided, there was a total weight gain of

From the Department of Medicine, Harper Hospital and Wayne University College of Medicine.

The 1-methyl-2-mercaptoimidazole (tapazol) was supplied by Dr. D. C. Hines of the Lilly Research Laboratories.

1. Stanley, M. M., and Astwood, E. B.: 1-Methyl-2-Mercaptoimidazole: An Antithyroid Compound Highly Active in Man, Endocrinology **44**: 588 (June) 1949.

2. Stanley, M. M., and Astwood, E. B.: Determination of the Relative Activities of Antithyroid Compounds in Man Using Radioactive Iodine, Endocrinology **41**: 66 (July) 1947; The Accumulation of Radioactive Iodide by the Thyroid Gland in Normal and Thyrotoxic Subjects and the Effect of Thiocyanate on Its Discharge, ibid. **42**: 107 (Feb.) 1948.

3. Hines, D. C.: Personal communication to the authors.

4 pounds, the blood pressure was 130 systolic and 80 diastolic and the thyroid was much reduced in size, but the exophthalmos was unchanged. The basal metabolic rate was + 20 per cent and the white blood cell count 7,200 with 61 per cent polymorphonuclear leukocytes. After ten weeks of treatment there was a further weight increase of 2 pounds, the thyroid was still smaller and just palpable and the exophthalmos was unchanged, but the basal metabolic rate was now + 1 per cent and the white blood cell count 6,800 with 66 per cent polymorphonuclear leukocytes.

Case 4.—J. McF., a white man aged 50, had had recurrent bronchial asthma for many years but was troubled by a persistent cough, worse when he was lying down, that resisted all forms of treatment. There was a partly substernal nodule in the right lower lobe of the thyroid. Manual tremor, warm moist palms and lidlag were present. The basal metabolic rate was + 18 per cent, the white blood cell count 7,550 with 50 per cent polymorphonuclear cells, the pulse rate 100 and the blood pressure 140 systolic and 70 diastolic.

The man was given 2 mg. of 1-methyl-2-mercaptoimidazole every eight hours for six weeks, at which time the tremor, nervousness and lidlag had disappeared, the palms were cool and dry, the thyroid nodule was smaller and the cough much improved. There was no change in weight, but the basal metabolic rate was — 9 per cent and the white cell count 6,250 with 67 per cent polymorphonuclear leukocytes. The dosage was reduced to 2 mg. every twelve hours for the next six weeks, and to the time of writing the patient has maintained the euthyroid state. He has gained a total of 7 pounds (3.2 Kg.); the blood pressure is 120 systolic and 70 diastolic, the pulse rate is 68 and the white blood cell count 6,300 with 64 per cent polymorphonuclear leukocytes.

TRANSFER TO 1-METHYL-2-MERCAPTOIMIDAZOLE

All the patients in this group were transferred to the new drug without disturbing the previous status. In making the change, 1 mg. of the new compound was substituted for each 25 mg. of the previously used propylthiouracil. Thus symptoms of 1 patient who had been receiving a daily maintenance dose of 50 mg. propylthiouracil continued under control with 2 mg. of the new antithyroid agent. Five patients who had been taking 100 mg. of propylthiouracil daily were given 4 mg. of the new drug instead. Three patients receiving 200 mg. of propylthiouracil daily required 4, 6 and 6 mg. of 1-methyl-2-mercaptoimidazole, respectively. One taking 300 mg. of propylthiouracil daily continued under control on 8 mg. of the new compound daily.

Patients in Relapse.—Symptoms of the 2 patients showing mild relapse, 1 after one year and the other after six months, after previous remission achieved with propylthiouracil, were readily controlled with 2 mg. of the new drug given every twelve hours in fifty-seven and fifty-one days, respectively.

SUMMARY

Of 18 patients with hyperthyroidism treated with a new antithyroid compound, 1-methyl-2-mercaptoimidazole, 3 with toxic diffuse goiter attained remission in approximately eight weeks. Two of these patients had been given 2 mg. of the drug every eight hours and 1 patient 5 mg. every twelve hours. Three patients with toxic adenoma reached remission in five to six weeks on a dosage of 2 mg. of the drug every eight hours in the first, 5 mg. every twelve hours in the second and 2 mg. every twelve hours in the third. Symptoms of 10 patients under treatment with propylthiouracil continued under control when 1 mg. of the new compound was substituted for each 25 mg. of the old. Two patients in mild relapse were readily controlled with 2 mg. of the new agent given every twelve hours for seven to eight weeks.

CONCLUSION

In the small group of patients observed, 1-methyl-2-mercaptoimidazole (tapazol) exhibited effective antithyroid activity closely resembling that of propylthiouracil but with a potency approximately twenty-five times greater.

Toxic reactions were not encountered, but more time and treatment of a larger number of patients will be required for assessment of this highly important factor.

3001 West Grand Boulevard.

Clinical Notes, Suggestions and New Instruments

MESENTERIC VASCULAR OCCLUSION

Extensive Resection of the Small Intestine with Survival

E. S. KOON Jr., M.D.
Lexington, Ky.

The case described herein is apparently the sixty-fifth report of successful surgical treatment of mesenteric vascular occlusion since 1895, when Elliot[1] performed an enterectomy with removal of 130 cm. of small intestine. The term "extensive," when applied to resection of the small intestine, has been indicative of the removal of lengths measuring 200 cm. or more. This limit was originally chosen because it was estimated that such a length constituted approximately one third of the small intestine and represented the extent of the small bowel that might be removed from a given patient with safety.[2]

Subsequent case reports have not borne out this contention. Bryant[3] reported on the length of the small intestine in 160 adults, revealing a wide variation from 10 feet (3.048 M.) to 28 feet 4 inches (8.636 M.) with an average of 20 feet 6 inches (6.248 M.). Consequently the amount of small intestine remaining after surgery is the important factor. In the case reported here, an estimated 6 feet (1.83 M.) of small bowel remained. Chodoff[4] reports the successful removal of 258 cm. of small bowel leaving only 4 inches (10.16 cm.) of jejunum and 4 inches (10.6 cm.) of ileum. The follow-up after three months showed a weight loss of 14 pounds (6.4 Kg.), and the patient was having four soft stools per day while on a high carbohydrate, medium protein, low fat diet. This patient died seven months postoperatively from auricular fibrillation and congestive cardiac failure. Meyer[5] removed all of the small bowel except 18 inches (45.72 cm.) of jejunum in addition to the ascending colon and right half of the transverse colon in a 19 year old white boy. Nine months later the patient complained only of two to three semiformed stools per day. Best results were obtained with a high carbohydrate, medium protein, low fat diet. Biochemical studies performed on a patient with 3 feet (0.91 M.) of small intestine showed that carbohydrate was as well utilized as in normal persons, whereas 75 per cent of protein and 55 per cent of fat were metabolized.[6]

REPORT OF CASE

A 73 year old white man was admitted to the hospital complaining of vague abdominal pain. Approximately 18 hours before admission he had the onset of a vague umbilical pain which was constant in nature with occasional cramplike exacerbations. The pain had slowly increased in severity and kept

1. Elliot, J. W.: The Operative Relief of Gangrene of the Intestine Due to Occlusion of the Mesenteric Vessels, Ann. Surg. **21**: 9 (Jan.) 1895.
2. Senn, N.: An Experimental Contribution to Intestinal Surgery, with Special Reference to the Treatment of Intestinal Obstruction, Ann. Surg. **7**: 1, 1888.
3. Bryant, J.: Observations upon the Growth and Length of the Human Intestine, Am. J. M. Sc. **167**: 499 (April) 1924.
4. Chodoff, R. J.: Mesenteric Vascular Occlusion: Case Report of Successful Resection of All but Eight Inches of Jejunum and Ileum, Ann. Surg. **131**: 440 (March) 1950.
5. Meyer, H. W.: Acute Mesenteric Artery Thrombosis, Arch. Surg. **53**: 298 (Sept.) 1946.
6. West, E. S.; Montague, J. R., and Judy, F. R.: Digestion and Absorption in a Man with Three Feet of Small Intestine, Am. J. Digest. Dis. **5**: 690 (Dec.) 1938.

the patient from sleeping the preceding night. There was concomitant anorexia without nausea or vomiting. He was chronically constipated, and on the previous evening he had taken 2 phenolphthalein tablets in a chocolate base (ex-lax®) and a "dose" of magnesium sulfate (epsom salts) without any resulting stools. The past history was noncontributory.

Physical examination revealed a well developed, well nourished man who appeared ill but in no acute distress. His blood pressure was 120 systolic and 80 diastolic, pulse rate 90, respirations 20 and temperature 99.8 F. The abdomen was slightly distended and tympanitic to percussion. There was some increased muscle resistance and tenderness in the right lower abdominal quadrant. Questionable referred tenderness to the epigastrium was noted. There were no palpable masses. Rectal examination revealed no masses or tenderness. The remainder of the physical examination showed nothing of significance.

The patient was admitted for further observation. Results of a proctoscopic examination for a distance of 25 cm. were essentially negative. A roentgenogram of the abdomen revealed borderline distention of the transverse colon and two loops of small bowel. The changes were not considered diagnostic. The results of laboratory work performed at the time of admission were as follows: red blood cell count 5,320,000, hemoglobin 16.3 Gm. and white blood cell count 12,250, with 79 per cent polymorphonuclear leukocytes and 6 per cent stab forms. The urine was normal.

There was a temperature elevation to 100.4 F. the day of admission, however the patient's signs and symptoms remained essentially unchanged. The following morning, almost twenty-four hours after entering the hospital, the patient fainted while in the lavatory. Blood pressure at that time was 100 systolic and 60 diastolic. His skin was pale and clammy. He complained of increased cramping pain in the umbilical region, and his abdomen was more distended and rigid. A roentgenogram of the abdomen showed the stomach to be full of gas and a small amount of small bowel distention in the upper part of the abdomen. The patient's state of shock rapidly became worse, and he was taken to the operating room with a blood pressure of 50 systolic and 0 diastolic.

With the patient under spinal anesthesia, the peritoneal cavity was examined and large amounts of grossly bloody fluid and clots were encountered and removed. Several loops of gangrenous small bowel protruded into the wound and were easily delivered from the abdomen. The mesentery was thickened with edema fluid. Viable small bowel was clamped proximad and distad to the gangrenous loops and cut across. The attached mesentery was clamped, cut and ligated. On further examination, the remaining part of the gastrointestinal tract appeared normal except for slight gaseous distention proximal to the resection. End to end anastomosis was carried out and the mesentery closed with interrupted sutures. The duodenum and remaining jejunum were estimated to measure approximately 2 feet (61 cm.) in length. The remaining ileum was an estimated 3 (91 cm.) to 4 feet (122 cm.) in length. A Miller-Abbott tube was inserted down to the point of anastomosis and the wound closed. Considering the poor condition of the patient at the beginning of the procedure, he withstood it well and was returned to his room conscious and with a normal blood pressure. He had received 1,500 cc. of blood during the operation.

The operative specimen measured 275 cm. and microscopically showed distinct inflammation and necrosis.

The patient's postoperative course was remarkably uneventful. His highest temperature reading was 102.2 F. (rectal) on the second postoperative day. He was maintained on parenteral fluids until the fourth day after operation when the Miller-Abbott tube was clamped off during the day and small amounts of fluid administered by mouth. The tube was finally removed three days later. Oral intake was gradually increased, and only once did the patient complain of discomfort after eating. Results of blood chemistry studies made postoperatively were within normal limits. He was dismissed fifteen days after operation having one to three semiformed stools per day.

A follow-up visit six months after operation revealed that the patient was doing his usual farm work without difficulty. He had maintained his normal weight without dietary regulation or restriction and had continued to have one to three semiformed stools daily.

SUMMARY AND CONCLUSION

1. A patient with mesenteric vascular occlusion survived the surgical removal of 275 cm. of small intestine. An estimated 6 feet (183 cm.) of small bowel remained.

2. The length of small bowel remaining after enterectomy is emphasized as the most important factor.

PEDUNCULATED BALL THROMBUS IN A HYPERTENSIVE HEART

HENRY A. STRADE, M.D.
New York

Ball thrombus of the heart is a rare pathologic entity.[1] The 35 cases reported to date have included both free and pedunculated thrombi as well as large vegetative thrombi occurring in several cases of subacute bacterial endocarditis. A precise classification, although desirable, is probably only of academic interest because the clinical observations are invariably similar regardless of the type of thrombus. To date, however, free ball thrombi have been found only in association with mitral stenosis and therefore probably deserve classification as a separate entity.[1a] For a review of the clinical observations the interested reader is referred to the excellent report of Schwartz and Biloon.[2] The outstanding signs are usually those of widespread and transient peripheral circulatory disturbances secondary to embolus, thrombosis or some degree of mitral valve occlusion with resulting gangrene of the affected parts.

The cause of free and pedunculated forms of auricular thrombi is by no means clear, but possibly these forms may be due to a combination of factors. In earlier cases the constant observation of left auricular thrombus in the presence of mitral stenosis led Von Ziemssen, in 1890, to postulate that mitral stenosis is necessary for thrombus formation.[3] Garvin[1b] believed that auricular fibrillation is an additional important factor because it causes incomplete emptying of the heart, which in turn favors formation and possible detachment of mural thrombi. Spain[1c] reported an interesting case of pedunculated left auricular thrombus associated with mitral stenosis which was diagnosed during life. Auricular fibrillation was absent, at least during the patient's hospital stay, and thrombus formation was thought to be secondary to left auricular endocarditis. Rheumatic endocarditis is known to occur especially in the left auricle[4]; since almost all ball thrombi also occur here, the relationship might be more than coincidental and could conceivably be of etiologic significance, as illustrated in Spain's case.

Von Ziemssen's postulate was shown to be untenable when a case of pedunculated left auricular thrombus in a hypertensive heart was reported in 1931[2] and again in 1935.[3] The latter case was extremely interesting in that the initial diagnosis, based on clinical and auscultatory observations, was rheumatic heart disease with mitral stenosis. To the best of my knowledge the case reported here represents only the third such case in the literature. The similarity of this case to the 2 previously reported cases is rather remarkable. The heart, in each of the earlier cases, weighed exactly 870 Gm.; in this case it weighed 875 Gm. In addition, the left auricular thrombus in each case was pedunculated; auricular fibrillation had been present, and the mitral cusps were normal. It would be premature at this time to assume that these 3 cases represent a separate pathologic entity. Worthy of note in the report which follows is a documented life span of thirty-two years subsequent to the first episode of cardiac decompensation.

REPORT OF CASE

History.—E. K., a white man aged 79, was readmitted to St. Luke's Hospital on Oct. 16, 1948 for the tenth time since

From the Department of Medicine, St. Luke's Hospital; formerly resident in medicine.

1. (*a*) Aronstein, C. G., and Neuman, L.: Ball Thrombus of the Heart: Report of a Case with Review of the Literature, Arch. Path. **27**: 907 (May) 1939. (*b*) Garvin, C. F.: Ball Thrombi in the Heart: Report of 3 Cases, Am. Heart J. **21**: 371, 1941. (*c*) Spain, D. M.: Ball Thrombus in the Heart, Ann. Int. Med. **19**: 144, 1943.

2. Schwartz, S. P., and Biloon, S.: The Clinical Signs of Occluding Thrombi of the Left Auricle, Am. Heart J. **7**: 84, 1931.

3. Von Ziemssen, cited by Kaplan, D., and Hollingsworth, E. W.: Pedunculated Thrombus of the Left Auricle Simulating Mitral Stenosis, J. A. M. A. **105**: 1264 (Oct. 19) 1935.

4. Cecil, R. L.: A Textbook of Medicine, ed. 6, Philadelphia, W. B. Saunders Company, 1943, p. 436.

1916 with symptoms of cardiac decompensation. At his first admission in 1916 a diagnosis of hypertensive cardiovascular disease with decompensation and ascites was made. Physical examination then revealed a blood pressure of 185 systolic and 110 diastolic and a heart that was enlarged by percussion to the anterior axillary line. Murmurs were not heard, but the second aortic sound was accentuated. The lungs were clear, and the liver and spleen could not be palpated. Ascites was present.

In the years which followed the patient continued under the care of his physician, and in 1939 he was admitted for the fourth time for hypertensive cardiovascular disease and decompensation. Electrocardiograms revealed partial auriculoventricular heart block. On his fifth admission in 1942 electrocardiograms revealed persistence of the incomplete auriculoventricular block together with a right bundle branch block. Auricular fibrillation was first noticed on a subsequent admission in 1943, with persistence of the right bundle branch block.

The patient was followed in the outpatient department from 1943 to 1946. During this time he remained in a state of chronic decompensation. He never responded to the usual cardiac regimen, and hospitalization was repeatedly recommended but always refused. He was not seen again until he was readmitted Oct. 16, 1948.

Physical Examination.—The patient was an elderly, obese white male sitting upright in bed with complaints of severe dyspnea and orthopnea. The lips, ears and nail beds were cyanotic. Blood pressure was 140 systolic and 85 diastolic. Examination of the chest showed a decided increase in the anteroposterior diameter. The chest was hyperresonant to percussion throughout, and the lungs were clear to auscultation. The heart was enlarged by percussion to the anterior axillary line with the maximal impulse in the sixth interspace in this line. There were no thrills or shocks. Heart sounds were weak and of poor quality, and the rhythm was that of auricular fibrillation. Systolic and diastolic murmurs were heard at the apex, and a short rough systolic murmur was heard over the aortic area. The abdomen was decidedly obese. The liver was palpated 6 cm. below the costal margin. Spleen and kidneys were not palpable. Ascites could not be demonstrated. Extremities revealed massive pitting edema of both legs. There was 2 plus pitting, sacral edema and minimal scrotal edema.

Urinalysis revealed a trace of albumin and frequent hyaline casts. A blood count was within normal limits. Urea nitrogen was 20.4 mg. per hundred cubic centimeters, and the erythrocyte sedimentation rate (Westergren) was 5 mm. per hour. Electrocardiograms showed auricular fibrillation, ventricular ectopic systoles and right bundle branch block. A roentgenogram of the chest on October 18 revealed great enlargement of the heart, chiefly in the transverse diameter. The left ventricular border reached the left chest wall. Infiltrative lesions which were seen in the region of the left hilum extending out to the periphery were consistent with bronchopneumonia.

The patient was given a milk diet, 3,000 cc. of fluids daily, scillaren 0.8 mg. three times a day and 2 cc. of meralluride sodium solution daily; he was placed in an oxygen tent. On this regimen, diuresis was satisfactory and the patient lost 11 pounds (5 Kg.) during the first forty-eight hours. On the second day he had a spiking fever (102 F.) and showed signs of bronchopneumonia at the base of the left lung. Moist rales were also heard at the right lung base at this time. He was given 100,000 units of penicillin every eight hours but grew steadily worse and disoriented and died on his fourth hospital day.

Necropsy Observations.—Necropsy was limited to abdominal incision. The left lung weighed 825 Gm., the right 1,125 Gm. All lobes revealed evidence of congestion and edema, with bronchopneumonia apparent in the lower lobe of the left lung. Many large pigment-filled cells were seen in the alveoli in the microscopic sections. The primary pulmonary arteries were large. Their lumens were almost completely occluded by lamellated firm thrombi, which were firmly attached to the intimal surfaces a short distance beyond the bifurcation and extending 2 to 3 cm. further. The primary arteries were estimated to be 75 per cent occluded by these thrombi, which did not extend into the peripheral arteries.

The heart weighed 875 Gm. There was decided dilatation of the left side of the heart. The myocardium was soft and flabby. The valve cusps showed no lesions and had the following circumferences: mitral 13.5 cm.; tricuspid 14.0 cm.; aortic 9.5 cm., and pulmonic 10.0 cm. The thickness of the left ventricle was 2.0 cm. and that of the right ventricle 0.5 cm. In the left auricle there was a thrombus measuring 4 by 3 by 3 cm. firmly attached to the superior endocardial surface by a pedicle 1.5 cm. in length. The thrombus was gray and lamellated; sections revealed some central greenish softening. The coronary arteries showed pronounced arteriosclerosis. The left coronary artery revealed a fresh thrombus which completely occluded the lumen. The liver manifested chronic passive congestion, cardiac cirrhosis and fatty changes. The spleen contained an old infarct in its lower portion.

The anatomic diagnosis was hypertensive heart disease, pronounced coronary arteriosclerosis, pedunculated thrombus of the left auricle, extensive myocardial and endocardial fibrosis, old pulmonary artery thrombi, bronchopneumonia of the left lower lobe, old infarct of the spleen and chronic passive congestion and cardiac cirrhosis of the liver.

SUMMARY

A case of pedunculated left auricular thrombus in a hypertensive heart is reported. This represents the third such case in the literature.

The presence of normal mitral valves in this case proves once again that mitral stenosis is not necessary for the formation of left auricular thrombus. Other possible etiologic factors are briefly discussed.

Council on Physical Medicine and Rehabilitation

REPORT OF THE COUNCIL

The Council on Physical Medicine and Rehabilitation has authorized publication of the following report.

HOWARD A. CARTER, *Secretary.*

BURDICK ELECTROCARDIOGRAPH, MODEL EK-1, ACCEPTED

Manufacturer: The Burdick Corporation, 635 Plumb Street, Milton, Wis.

The Burdick EK-1 is a direct-writing electrocardiograph which produces records by means of an electrically heated stylus tracing on heat-sensitive paper. The instrument weighs 18 Kg. (39 pounds) and measures 32 by 41 by 23 cm. (12½ by 16 by 9 inches). The shipping weight is 23.5 Kg. (54 pounds).

Burdick Electrocardiograph Model EK-1

The following additional description is quoted from a statement by the firm: "The instrument operates on a 117 volt, 60 cycle, alternating current line. The power consumption with the record mechanism in operation is 85 watts. The idling power consumption is 60 watts. The instrument is so designed that it will maintain its accuracy over a voltage range of from 105 to 130 volts. The selection of patient leads is controlled by a switch in the instrument eliminating the necessity of shifting leads on the patient. (The exception of course being the change of position of the exploring electrode in multiple chest leads.) The internal standard is a Weston standard cell Model 3 Type 4. This cell has a voltage of 1.019 volts and by the use of 1 per cent precision resistors in the standardizing network a one-millivolt standard is obtained."

Both the electrophysical and clinical tests were done in laboratories acceptable to the Council, and evidence of satisfactory construction and operation was obtained. The Council on Physical Medicine and Rehabilitation voted to include the Burdick Electrocardiograph, Model EK-1, in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORT TO THE COUNCIL

The Council has followed with interest the development of various flavonoid substances alleged to have the property of increasing capillary resistance but does not believe there is conclusive evidence available to substantiate the claims advanced for these drugs. The following report by William G. Clark and Eaton M. MacKay, which indicates that rutin and related flavonoid compounds are probably destroyed in the gastrointestinal tract, furnishes an additional basis for skepticism. However, even though these compounds may not be absorbed as such in significant amounts, this in itself would not prove that they exert no action. It is conceivable that one or more breakdown products might be absorbed and produce the effects which have been reported. The Council has adopted this report for publication in the hope that it will stimulate investigators to establish by objective and critical experiments whether or not oral administration of any of these substances or their breakdown products produces significant pharmacologic effects.

R. T. STORMONT, M.D., *Secretary.*

THE ABSORPTION AND EXCRETION OF RUTIN AND RELATED FLAVONOID SUBSTANCES

WILLIAM G. CLARK, Ph.D.
and
EATON M. MacKAY, M.D.
With the Technical Assistance of Mary Jordan
La Jolla, Calif.

Although there is an extensive literature on the therapeutic effects of flavonoid substances, erroneously referred to as vitamin P, such as citrin,[6] rutin, hesperidin and related compounds and crude extracts (e. g., of citrus peels and rose hips), little has been published on their absorption, metabolism and excretion. This becomes important in connection with claims of the vitamin-like nature of the substances, and the widespread use of proprietary preparations containing rutin and related compounds for pathologic conditions involving capillary fragility and hemorrhage, hypertension and radiation disease.

Many of the flavonoids are common plant pigments, along with the related anthocyanins of grapes, berries, beets, citrus and other fruits, vegetables and flowers.

It has been demonstrated that anthocyanin pigments such as cyanidin and delphinidin are not appreciably absorbed on oral ingestion by most higher animals, and when injected parenterally in animals they are not metabolized, being renally excreted unchanged.[1] Similar observations have been made on flavonoid and related pigments when injected into animals and human subjects.[2] If such plant pigments were absorbed from the intestine and not metabolized, it would be expected that the urine would be colored after ingestion of foods such as grapes, wine, berries and beets; not only does this not occur normally in adult humans, but it is a common observation that the feces are colored after ingestion of these foods in large amounts.[3] Human infants may excrete pigmented urine after ingesting anthocyanin-containing vegetable matter. Fukuda [4] and Kono [5] claimed that complete urinary excretion occurs within 20 hours after the oral administration or after direct introduction into intestinal segments in situ of the flavonoids, quercitrin, quercetin, morin, kaempherol and rutin in fasted rabbits.[6]

The nonspecific "alkali red" test [7] was used to identify the compounds, which may invalidate this work considerably if one assumes there is some validity in these experiments. However, it still is possible that the rabbit differs in this respect from other species, as suggested by Horwitt's observation [1] that orally administered anthocyanin is excreted by the rabbit but not by dogs and rats, which is in agreement with Czimmer,[8] who observed no urinary excretion of a quercetin glycoside fed to rats. Garino [2b] fed quercitrin (quercetin-3-rhamnoside) and rutin (quercetin-3-rutinoside) to dogs and claimed to have recovered the unaltered compounds in the urine. Opposed to this finding are the analytic data of Field and Rekers,[9] which showed a negligible urinary excretion of rutin fed to dogs in amounts ranging from 0.3 to 0.5 Gm. daily, and of Porter, Dickel and Couch,[10] who recovered only negligible traces of rutin from the urine of human subjects fed 0.6 to 2.25 Gm. daily for one to two weeks.

Gero recovered about 20 per cent from the urine of patients fed 50 mg. of epimerized *d*-catechin (a flavane), and 65 per cent after intraperitoneal injection in guinea pigs. Kirtley and Peck [11] concluded that "methylated hesperidin chalcone" is not excreted in the urine as such, after oral doses as high as 15 Gm. daily in man. Scarborough [12] stated that the oral administration of "vitamin P" leads to an increased excretion of glucuronic acid in man, but no data were given.

If flavonoids and anthocyanins are excreted unchanged after parenteral injections, as shown by the various workers already quoted,[13] then one would expect them to be similarly excreted in unaltered form if they are absorbed from the intestine. If they are not absorbed appreciably by man, they should either appear in the feces or be destroyed by the intestinal flora, some of which are known to contain enzyme systems capable of oxidizing phenolic substances.

Furthermore, evidence confirming the suspicion that they are not appreciably absorbed might explain the conflicting reports of the various experimental and

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The present address of Dr. Clark is General Medical Research Service, Veterans Administration Center, Los Angeles 25.
From the Scripps Metabolic Clinic, La Jolla, Calif. This investigation was supported in part by the Division of Research Grants and Fellowships of the National Institutes of Health, United States Public Health Service, and the Eli Lilly Company.

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therapeutic effects of these substances, since in many instances the routes of administration differed; in nearly all the reports in American literature the drugs were given orally to human subjects. It would also strengthen the denial [14] of the claim [15] that some of the flavonoid substances are vitamin-like (vitamin C_2) in nature. Accordingly experiments were designed to attempt to clarify the question of the absorption, metabolism and excretion of the flavonoids and related plant pigments.

METHODS AND RESULTS

I. *Chemical Methods.*—A. Free and Conjugated Phenols: Free and conjugated phenols were determined colorimetrically by an adaptation of Marenzi's [16] modification of the diazotized *p*-nitroaniline method of Theis and Benedict.[17]

1. Urine. The method gave 98 to 100 per cent recovery of 0.01 to 0.02 mg. of phenol, rutin and related flavonoids added to urine.

2. Stools. Flavonoids added to homogenized acidified stool samples, diluted with ethyl alcohol, evaporated to dryness and extracted with methyl alcohol were not satisfactorily recovered.

B. Borocitrate Test: The borocitrate test, developed by Wilson [18] depends on the formation by boric acid under anhydrous conditions of a yellow complex with certain flavonoids, which is intensified by anhydrous citric acid. It was used by Kirtley and Peck [11] in the excretion studies already mentioned.

1. Urine. Ten cubic centimeters of urine, with 0.5 to 1.0 mg. of flavonoid, were slightly acidified with hydrochloric acid and evaporated to dryness; 10 cc. absolute ethyl alcohol were added and the solution boiled nearly to dryness and transferred to a 12 cc. calibrated centrifuge tube, which then was filled to the 10 cc. mark with absolute ethyl alcohol and centrifuged. Five cubic centimeters of the supernatant were evaporated to dryness in a beaker and desiccated, and 10 cc. glacial acetic acid were added. Duplicate 1 cc. aliquots were added to Klett tubes containing 5 cc. of Wilson's citric acetone reagent and 5 cc. of the boric-acetone reagent. After standing 10 minutes, they were read in the Klett spectrophotometer with a 420 filter, against urine-reagent blanks. Recoveries ranged from 96 to 99 per cent.

2. Stools. Twenty grams of fresh human stool were made up to 200 cc. with water, acidified with a few drops of concentrated hydrochloric acid and divided into two portions of 100 cc. each. Rutin, 100 mg., was added to one and the other left as a blank. The samples were either lyophilized or evaporated to dryness on the steam bath in an evaporating dish under a stream of air, pulverized, transferred to a Soxhlet thimble, reflux-extracted with methyl alcohol for four hours and the extract diluted to 100 cc. with methyl alcohol. Ten cubic centimeters of 1:10 dilution in methyl alcohol were evaporated to dryness, desiccated in vacuo or under infra-red and taken up in 10 cc. glacial acetic acid.

One cubic centimeter (0.1 mg.) aliquots were used for the borocitrate color development. The stool sample without added rutin, and similarly treated, was used for color blanks. The recovery averaged 93 to 95 per cent. In a second method, the Soxhlet extraction was substituted for extraction of the evaporated stool sample with 100 to 150 cc. of hot ethyl alcohol on the steam bath for two hours, replacing the evaporated alcohol. Recovery was 100 per cent.

3. Gastrointestinal contents. The animal intestinal absorption experiments involved analysis of the flavonoids recovered from the stomach and intestinal tract, the entire organ being removed, minced and extracted. The method was adapted from MacKay and Bergman's [19] modification of Cori's [20] method for intestinal absorption studies.

Amounts of 50 to 100 mg. of drug were orally gavaged to fasted rats or guinea pigs with or without previous ligation of the rectum to prevent possible loss in the event of drug-induced diarrhea. At 0 hours (for a "blank" recovery) and at various times up to 8 hours, the cardiac and pyloric ends of the stomach and the intestine from the pyloric valve to the ileocecal valve, or sometimes to the lower part of the rectum, were clamped off and the stomach and intestine removed separately, minced and extracted. If water soluble, the extraction was made with hot, acidified water, otherwise hot, acidified ethyl alcohol, on the steam bath for an hour or more.

The borocitrate method gave up to 98 per cent recovery from the extracts, depending on the drug used and whether or not the cecal contents were included, which gave interfering colors.

C. The Aluminum Test: Several methods have been described in the literature for the determination of small amounts of aluminum by its ability to form colored complexes with polyphenols, such as quercetin.[21] Porter, Dickel and Couch,[10] reversing this process, examined the urine for rutin by a colorimetric determination of the aluminum complex of rutin, first separating and concentrating the rutin from other urinary pigments by adsorption on aluminum hydroxide gel which was washed. In our hands, this method gave 95 to 100 per cent recoveries from certain flavonoids added to urine but not from stool samples and tissues (60 to 70 per cent).

D. Glucuronide Tests: Glucuronide tests for possible conjugates of flavonoids in urine were run, with an adaptation of the combined methods of Jarrige [22] and of Florkin,[23] details of which will be published soon. Briefly, it consists of forming conjugates of the free (by acid hydrolysis of the conjugated) glucuronic acid with highly purified naphthoresorcinol, using potassium persulfate as a catalyst and in a boiling acid medium (six normal hydrochloric acid), cooling in ice, adding a detergent to prevent flotation of the fine precipitate; centrifuging, discarding the supernatant, washing, drying in vacuo, shaking up the dry naphthoresorcinol

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complex with benzene or ethylene chloride at room temperature and determining the color intensity in the Klett with a green (560) filter. The sensitivity is about 1 microgram per cubic centimeter; the specificity is high (no interference by hexoses, pentoses, keto-acids or aldehydes), and the recovery of microgram amounts from 10 cc. of urine is of the order of 96 per cent.

E. Muconic Acid: Benzene and phenolic substances have been shown to undergo ring cleavage in vivo, to form, among other things, muconic acid.[24] Consequently, urine muconic acid was tested for by the method of Drummond and Finar [25] in one instance after the ingestion of a very large dose of a flavonoid by a human subject.

F. Qualitative Tests: In order to test some of the urine specimens for traces of flavonoids after oral administration, recourse was had to a few sensitive qualitative color tests.

1. Ferric chloride test for phenols. A few drops of 1 per cent ferric chloride are added to a few cubic centimeters of urine. An olive or green color usually indicates the presence of the particular flavonoids investigated, with some exceptions.

2. Cyanidin test for flavonoids. Reddish to violet colors occur when an ethanol solution of certain flavonoids is added to an equal volume of concentrated hydrochloric acid and metallic magnesium is added.

3. "Chalcone" test. In this test chalcones form bright orange or red colors with concentrated sulfuric acid.

II. *Physiological Experiments.*—A. Human Subjects: 1. A 100 Kg. subject ingested 5 Gm. of rutin [26] in one dose (50 mg. per kilogram), and the 24 hour urine specimen was subjected to fractionation for various tests. The urine was made to 10 per cent in hydrochloric acid and continuously extracted with an equal volume of ether in a liquid extractor for 24 hours. Residues of large aliquots (50 cc.) of the ether layer gave negative borocitrate and cyanidin reactions. The aqueous layer was boiled on the steam bath for 90 minutes, to hydrolyze possible conjugates, and reextracted with ether, and again similar residues gave negative reactions. The aqueous layer was lyophilized and extracted with methyl alcohol in a Soxhlet until colorless (six hours). Both the residue and the extract gave negative borocitrate and cyanidin reactions.

2. Four subjects ingested in a single dose 50 mg. of rutin per kilogram of body weight, and the 24 hour urine specimens were tested for free and total phenols by the *p*-nitroaniline method and by the borocitrate test for one day before and after the subject took the rutin. The amounts excreted averaged 0.5 per cent of the amount fed, which is within the limits of error of the methods and can be considered negligible.

3. Stool and urine specimens were collected from 2 subjects for two days before and three to four days after ingestion of rutin, 50 mg. per kilogram. Each stool and urine specimen was analyzed by three different tests, *p*-nitroaniline (stool), borocitrate and aluminum. The analyses showed no or negligible amounts of rutin in the stool or the urine.

4. One subject ingested 50 mg. per kilogram of body weight of "methylated hesperidin chalcone." [27] The 24 hour urine specimens were collected for five days before and four days after and analyzed for free and total phenols by the *p*-nitroaniline method, the borocitrate method, free and conjugated glucuronic acid, muconic acid and qualitatively by the ferric chloride and cyanidin tests. The results showed no indication of urinary excretion of the drug or its possible metabolites.

5. A patient with a history of duodenal ulcers and gastric resection, whose urine contained beet anthocyanin,[28] was selected as being likely to absorb flavonoids, since these compounds are not chemically unrelated. The 24 hour urine specimens were collected one day before and after ingestion of 1 Gm. of rutin and analyzed for free and total phenols, by the borocitrate test, for free and conjugated glucuronic acid and by the cyanidin test. There was no increase in any of the tests over the pre-rutin level, under the experimental conditions employed.

B. Animals: 1. Intestinal absorption in rats. Thirty-six hour fasted male rats of the Slonaker strain, 6 rats per group, average body weight 200 Gm., were divided into five groups and each rat orally given 100 mg. (5 cc. of 2 per cent solution or suspension) of: group 1, rutin in 50 per cent propylene glycol; group 2, the soluble sodium salt of quercetin-6'-sulfonic acid [29] in water; group 3, rutin methyl glucamine (1 part rutin reacted with 0.7 parts methyl glucamine) in water, and group 4, "methylated hesperidin chalcone" in water. The fifth group served as controls. Representative rats were sacrificed immediately after gavaging and at various times thereafter up to eight hours and the intestinal absorptions determined as described earlier. The rutin-fed rats' minced organs and their contents were extracted with hot ethyl alcohol, while the proteins of the others were first precipitated with trichloracetic acid, before extraction with ethyl alcohol in the rutin methyl-glucamine rats and with water in the remainder. After an hour on the steam bath, the extracts were made up to 100 cc. with ethyl alcohol (water in the case of the chalcone and methyl-glucamine) and filtered. Two cubic centimeter aliquots of the filtrates were evaporated to dryness and analyzed by the borocitrate test. After 30 minutes the soluble rutin methyl-

TABLE 1.—*Intestinal Absorption of Rutin, Rutin Methyl Glucamine and Quercetin Sulfonate in the Rat*

Drug	Hours	Mg. Recovered: Stomach	Gut	Total	Conclusions and Remarks
Rutin-methyl-glucamine	0	73	14	87	Recovery at "0" hours no greater than subsequent figures; stomach empties and gut content increases, but total remains constant; indicates no absorption
	1.5	20	67	87	
	1	29	55	84	
	2	..	64	..	
	4	15	83	98	
	8	2	86	88	
Rutin in propylene glycol	0	72	21	93	Propylene glycol delays stomach emptying; total recoveries the same as at "0" hours, indicating no absorption
	1.5	52	35	87	
	1	43	46	89	
	4	45	45	90	
	8	48	46	94	
Quercetin-sulfonate	0	27	1	28	Very poor recovery at "0" hours; nevertheless the total recovered amount decreases, indicating binding, absorption or destruction (see urinary excretion experiments)
	1.5	17	1	18	
	1	19	1	20	
	2	16	2	18	
	4	1	3	4	
	8	1	1	2	

24. Williams, R. T.: Detoxication Mechanisms, New York, John Wiley & Sons, Inc., 1949.
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26. Supplied by Dr. W. G. Bywater, S. B. Penick Company, New York.
27. Supplied by Mr. A. J. Lorenz and Mr. W. E. Baier of the California Fruit Grower's Exchange, Los Angeles and Ontario, Calif.
28. Dr. James W. Callaway of this clinic made the urine collections and the observation that the patient excreted anthocyanins.
29. Supplied by Dr. W. G. Bywater, S. B. Penick Company.

glucamine had dissociated into typically insoluble rutin in the intestine.

The hesperidin chalcone and quercetin sulfonate recoveries at 0 hour were very poor, possibly because of inadequate extraction by the hot water. The rutin and rutin methyl-glucamine recoveries were better. The results are summarized in table 1.

2. Urinary excretions. (*a*) Four groups of 4 unfasted rats per group, average body weight 255 Gm. were caged by groups and each rat orally gavaged with 10 cc. of water containing: group 1, nothing; group 2, 125 mg. of rutin suspension (approximately 500 mg. per kilogram); group 3, 125 mg. of sodium quercetin-6'-sulfonate, and group 4, 125 mg. of rutin hexamethylenetetramine (urotropin) soluble complex (10 parts rutin plus 2 parts urotropin in 50 parts water, boil 20 minutes, lyophilize). The urine specimens were collected for six hours. Analyses were made for free and total phenols, free and conjugated glucuronic acid, by the borocitrate test and qualitatively by the sulfuric chalcone test, the cyanidin test and the ferric chloride test. The results are summarized in table 2.

TABLE 2.—*Urinary Excretion of Flavonoids by Rats*

Group	Total Phenol * †	Borocitrate *	Conjugated Glucuronic *	Cyanidin Test ‡	Chalcone Test §	Ferric Chloride Test ‖	Urine Color
Controls	...	...	...	Neg.	Neg.	Neg.	Light yellow
Rutin	Negligible	0.2	0.6	Neg.	Neg.	Neg.	Light yellow
Quercetin-sulfonate	2.5	1.3	2.3	Neg.	Neg.	Pos.	Orange
Rutin-Urotropin	0.6	0.4	2.0	Neg.	Neg.	Pos.	Light yellow

* Percentage of fed drug excreted.
† Expressed as equivalents of phenol.
‡ Two cubic centimeters of urine, 2 cc. absolute ethyl alcohol, 2 cc. of concentrated hydrochloric acid and magnesium shavings.
§ Urine, concentrated sulfuric acid, 1:1.
‖ Two drops, 1 per cent ferric chloride to 2 cc. urine.

It was concluded from this that the amounts excreted were within the limits of error of the methods used. With the soluble quercetin sulfonate, the untreated urine was more pigmented than the treated urine, and the ferric chloride test gave a faint green color, indicating a trace (less than 1 mg.) of the compound probably was excreted. The rutin-urotropin dissociated in the intestine to insoluble rutin, and the urine contained formaldehyde, indicating absorption of the urotropin alone.

(*b*) Nine 24 hour fasted male rats, average body weight 200 Gm. were divided into three groups. The colons were ligated to prevent contamination of urine by fecal contents in the event of diarrhea. The rats of group 1 received 500 mg. per kilogram of body weight of the quercetin sulfonate by oral gavage; group 2 received 500 mg. per kilogram of "calcium flavonate glucoside,"[30] and group 3 was fed water, serving as controls. The rats were caged together in groups and the urine collected for 24 hours.

The quercetin sulfonate urine, as before, gave a positive (green) ferric chloride reaction. The borocitrate tests indicate that less than 5 per cent of the fed amounts of quercetin sulfonate and calcium flavonate are excreted, which is close to the limits of analytic error.

(*c*) The aforementioned experiment was repeated, with the same drugs and, in addition, the soluble sodium salt of esculetin-4-carboxylic acid. The 24 hour urine specimens were analyzed by the borocitrate method. Less than 3 per cent of the fed dose of the quercetin sulfonate and esculetin derivative were excreted, with no calcium flavonate at all. The 3 per cent is within the limits of error of the method.

(*d*) The experiment was repeated, but with animals with unligated colons and the fairly soluble drugs citrin,[31] gossypin,[32] xanthorhamnetin[33] and "methylated hesperidin chalcone." In addition, 100 mg. of "calcium flavonate glucoside" was orally gavaged to each of two 24-hour-fasted guinea pigs, average body weight 400 Gm., with 2 others as controls.

The 24 hour collected urine specimens were analyzed by the aluminum chloride method, except in the case of the methylated chalcone, which responds better to the borocitrate test.

There was less than 5 per cent of the fed dose of drugs excreted by the rats, which is within the analytic error. There was no indication in the guinea pig of excretion of the calcium flavonate.[34]

C. Stool Incubation Experiments: Since these data indicate little or no urinary or fecal excretion of the compounds or likely degradative products or conjugates in humans, it seemed logical to determine whether the compounds might be destroyed by the fecal flora.

1. One hundred cubic centimeters of solution was made with 10 Gm. of fresh human stool and water and homogenized, and 100 mg. of rutin were added. This was incubated at 37 C. for 48 hours, with occasional stirring. It was then lyophilized; the dry powder was extracted with petroleum ether in a Soxhlet until colorless, then with chloroform, followed by methyl alcohol. The methyl alcohol extract was diluted 1:200 with methyl alcohol, and aliquots of this were analyzed by the aluminum method. No rutin was found.

2. The experiment was repeated, with a second patient's stool sample. One hundred milligram duplicates of the lyophilisate were extracted with hot glacial acetic acid, centrifuged, the supernatants diluted 10 times with glacial acetic and 1 cc. aliquots analyzed by the borocitrate method. More than 95 per cent destruction of rutin had occurred.

3. From stool sample 1, after incubation, the only micro-organisms which could be isolated were Staphylococcus and a gram-negative rod, distinct from the coliform bacteria. One hundred cubic centimeters of 24 hour dextrose-broth cultures of these two organisms were incubated with 100 mg. rutin. No destruction of rutin occurred.

4. Twenty grams of fresh stool samples pooled from 5 patients were homogenized, made up to 200 cc. with water and divided into two lots of 100 cc. each. To one was added 100 mg. of rutin, and the other served

30. A soluble citrus-derived flavonoid supplied by the California Fruit Growers' Exchange.

31. A semipurified soluble flavonoid prepared from citrus peel concentrates by Dr. A. N. Wick.

32. Supplied by Dr. T. R. Seshadri, Department of Chemistry University of Delhi, Delhi, India.

33. Supplied by the S. B. Penick Company, New York. Solubilized before feeding by adjusting the *p*H to 10 with sodium hydroxide.

34. This may throw doubt on our statement (Clark, W. G.; Uncapher, R. P., and Jordan, M.: Science **108**: 629 [Dec.] 1948) that calcium flavonate fed to guinea pigs protects them from death from total body roentgen irradiation.

as a control. After incubation at 37 C. for 48 hours, the whole samples were lyophilized, the dry powders extracted with 100 to 150 cc. hot ethyl alcohol for two hours, made up to 200 cc. with ethyl alcohol, 2 cc. aliquots (1 mg.) evaporated, desiccated and taken up in glacial acetic acid for the borocitrate test. One hundred per cent recovery of rutin added to unincubated stool samples was obtained the same day; but in the incubated sample there was 83 per cent loss.

5. This experiment was repeated, substituting dextrose-broth for water; 87 per cent rutin was recovered. The experiment was repeated, incubating samples in water and in culture medium with essentially the same results: rapid destruction in water-stool homogenate, not much in broth. This suggests that in the presence of broth there may be an overgrowth of organisms which do not destroy rutin but which suppress the growth of rutin-destroying ones. The point was not pursued further.

It may be concluded that when rutin is incubated with human stools in water (but not broth) it is destroyed. This may explain why, in the human feeding experiments, flavonoids were not found in the stools.

COMMENT

It was found in human experiments that urinary excretion following large oral doses (50 mg. per kilogram of body weight) of flavonoid compounds is negligible, that these materials are not recoverable from the stools and that rutin is destroyed when incubated in an aqueous stool suspension. In animals the percentage of the fed doses which were (*a*) absorbed from the intestine and (*b*) excreted in the urine were negligible, some of the fed compounds being fairly completely recoverable from the gastrointestinal tract.

The flavonoids studied included: rutin, its soluble complexes with methyl glucamine and methenamine, "methylated hesperidin chalcone," the sodium salt of esculetin-4-carboxylic acid and of quercetin-6′-sulfonic acid, "calcium flavonate glucoside," citrin,® gossypin and xanthorhamnetin.

The results suggested that a trace (less than 1 per cent) of the fed dose of sodium quercetin-6′-sulfonate may be absorbed and excreted by rats.

The quantitative recoveries were not accurate to more than a small percentage, although they were sensitive to a few micrograms; hence it cannot be said that very minute amounts of the flavonoids were not absorbed. The more soluble flavonoids were no better absorbed than the more insoluble ones, such as rutin. The soluble complexes of rutin dissociated to the typically insoluble rutin in the intestine.

The results support the cumulative evidence that it is unlikely that (1) these substances are vitamin-like and (2) they exert any specific chemical or therapeutic effect.

Evidence presented elsewhere [35] showed that when parenterally administered these compounds cause just as much decrease in adrenal ascorbic acid as epinephrine or pituitary adrenocorticotropic hormone and thus may elicit a nonspecific stress or "alarm reaction," which may explain many of the physiologic and pharmacologic nonspecific effects which they are said to exert.

35. Clark W. G.: Paper read before the fall meeting of the American Physiological Society, 1949: to be published.

Council on Foods and Nutrition

ACCEPTED FOODS

The following products have been accepted as conforming to the rules of the Council.

JAMES R. WILSON, M.D., *Secretary.*

Beech-Nut Packing Company, Canajoharie, N. Y.

BEECH-NUT STRAINED SWEET POTATOES. Ingredients: Sweet potatoes, salt and sufficient water for preparation.

Analysis (submitted by manufacturer).—Total solids 27.30%, moisture 72.70%, ash 0.97%, fat (ether extract) 0.19%, protein (N × 6.25) 0.77%, crude fiber 0.50%, carbohydrates other than crude fiber (by difference) 24.87%.

Vitamins and Minerals	Mg./100 Gm.
Carotene	0.076
Thiamine	0.037
Riboflavin	0.017
Nicotinic acid	0.350
Calcium	19
Phosphorus	27
Iron (total)	0.67
Iron (available)	0.42
Copper	0.27

Calories.—1.04 per gram; 29.5 per ounce.

Use.—For use in the feeding of infants, convalescents and others requiring a soft diet.

BEECH-NUT STRAINED GARDEN VEGETABLES. Ingredients: Peas, carrots, spinach, salt and water sufficient for preparation.

Analysis (submitted by manufacturer).—Total solids 16.16%, moisture 83.84%, ash 1.23%, fat (ether extract) 0.41%, protein (N × 6.25) 2.84%, crude fiber 1.13%, carbohydrates other than crude fiber (by difference) 10.55%.

Vitamins and Minerals	Mg./100 Gm.
Carotene	0.099
Thiamine	0.084
Riboflavin	0.075
Nicotinic acid	0.850
Calcium	50
Phosphorus	56
Iron (total)	1.30
Iron (available)	1.06
Copper	0.11

Calories.—0.57 per gram; 16.2 per ounce.

Use.—For use in the feeding of infants, convalescents and others requiring a soft diet.

Clapp's Baby Food Division, American Home Foods, Inc., Rochester, N. Y.

CLAPP'S JUNIOR FOODS—APRICOTS AND APPLES. Ingredients: Apricot puree, apples and sugar.

Analysis (submitted by manufacturer).—Total solids 16.38%, ash 0.14%, fat (ether extract) 0.09%, protein (N × 6.25) 1.57%, crude fiber 1.07%, carbohydrates other than crude fiber (by difference) 13.51%.

Vitamins and Minerals	Mg. per Hundred Grams
Vitamin A	0.07
Thiamine	0.01
Riboflavin	0.012
Ascorbic acid	1.12
Niacin	0.04
Calcium	6.30
Phosphorus	10.70
Iron	0.65
Copper	0.09

Calories.—0.61 per gram; 17.35 per ounce.

Use.—For use in the feeding of older infants and young children.

Mead Johnson and Company, Evansville, Ind.

LACTUM. Ingredients: Evaporated Whole Milk and Dextri-Maltose® with added vitamin D (irradiated ergosterol).

Analysis w/v (submitted by manufacturer).—Water 70.0%, protein (N × 6.38) 5.3%, fat 5.2%, carbohydrate: from milk 7.0%, from Dextri-Maltose® 10.1%.

Vitamins and Minerals	Per 100 Ml.
Calcium	220 mg.
Phosphorus	200 mg.
Iron	0.2 mg.
Vitamin D	103 U.S.P. units

Calories.—1.35 per ml.; 40 per fluid ounce.

Use.—For use in infant feeding.

DALACTUM. Ingredients: Evaporated Whole Milk, Skim Milk, Dextri-Maltose® with added vitamin D (irradiated ergosterol).

Analysis w/v (submitted by manufacturer).—Water 68.0%, protein (N × 6.38) 5.5%, fat 2.7%, carbohydrate: from milk 7.1%, from Dextri-Maltose® 15.3%.

Vitamins and Minerals	Per 100 Ml.
Calcium	220 mg.
Phosphorus	200 mg.
Iron	0.2 mg.
Vitamin D	103 U.S.P. units

Calories.—1.35 per ml.; 40 per fluid ounce.

Use.—For use in infant feeding.

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AUSTIN SMITH, M.D.

Associate Editor
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SATURDAY, AUGUST 19, 1950

REGISTRATION OF PHYSICIANS FOR MILITARY SERVICE

At a meeting on August 12 the Board of Trustees of the American Medical Association endorsed the principles of several bills pending in Congress which provide for the registration and induction into service of certain technical and specialist personnel, including physicians. In taking this position, the Board asserted that the Association will make every effort to see that adequate medical care is provided for members of the armed forces. The Board believes that any legislation of this type which may be enacted should provide so far as physicians are concerned, for call in the following order:

1. Those who participated as students in the Army specialized training program or similar programs administered by the Navy, and persons who were deferred from service during World War II for the purpose of pursuing a course of instruction leading to medical education, and who have had no active duty as commissioned officers.

2. Those who have been deferred previously for other than physical disability and those previously rejected for physical disability who may be found fit on the basis of present physical requirements.

3. Those who participated in the Army specialized training program or similar programs administered by the Navy and who have served on active duty as commissioned officers for less than 21 months (exclusive of the time spent in postgraduate training).

4. Those who have had less than 90 days' prior active honorable military or naval duty.

5. Those whose total active honorable military or naval duty is less than 21 months.

SULFHYDRYL COMPOUNDS AND EXPERIMENTAL DIABETES

The discovery that alloxan will produce an experimental diabetes similar to diabetes mellitus in man has proved valuable in the study of fundamental alterations in carbohydrate metabolism in this pathologic condition. Recently, the relation of sulfhydryl compounds, particularly cysteine and glutathione, to experimental alloxan diabetes has received attention. One of the first demonstrations of this relation was that of a group of workers [1] at Western Reserve University, who reported that glutathione or cysteine given intravenously with alloxan prevented the development of diabetes. BAL (2,3-dimercaptopropanol) and thioglycolic acid were also effective, whereas methionine and thiourea were not.[2] It was found necessary to administer the sulfhydryl compounds within one to three minutes of the injection of alloxan in order to obtain the preventive effect. These investigators [3] suggest that cysteine and glutathione may reduce alloxan to dialuric acid, a nondiabetogenic substance, and thus exert the observed protective action. They further suggest that alloxan may combine with, and therefore block sulfhydryl groups of, some enzyme essential for normal carbohydrate metabolism and in this manner exert its diabetogenic effect. Of interest in this connection is the recent claim [4] that reduced glutathione alleviates the temporary diabetes produced in human subjects by the administration of pituitary adrenocorticotropic hormone (ACTH).

Other evidence from three different types of investigation likewise implicates the sulfhydryl group with experimental diabetes. One of these studies [5] reveals that the administration of a sodium-deficient diet to rats results in a decrease in the blood glutathione level and an increased susceptibility to the diabetogenic action of alloxan. Another [6] states that dehydroascorbic acid and, to a lesser extent, dehydroisoascorbic acid are diabetogenic, perhaps by destroying sulfhydryl groups of enzymes essential to normal carbohydrate utilization. The third report [7] is an unconfirmed claim that uric acid is diabetogenic in rabbits in which the blood glutathione level is reduced by the feeding of a cysteine-deficient diet.

Although the foregoing studies individually are perhaps in need of further careful and critical evaluation before a conclusion can be drawn, taken collectively they indicate a fundamental role of the sulfhydryl group in normal carbohydrate metabolism and suggest possible impairment of the process in the diabetic organism. Further studies of this basic problem should aid in the elucidation of the underlying biochemical lesion in, and thus the rational control of, diabetes in man.

1. Lazarow, A.: Proc. Soc. Exper. Biol. & Med. **61**: 441, 1946.
2. Lazarow, A.: Proc. Soc. Exper. Biol. & Med. **66**: 4, 1947.
3. Lazarow, A.; Patterson, J. W., and Levey, S.: Science **108**: 308, 1948.
4. Conn, J. W.; Louis, L. H., and Johnston, M. W.: Science **109**: 279, 1949.
5. Grunert, R. R., and Phillips, P. H.: J. Biol. Chem. **181**: 821, 1949.
6. Patterson, J. W.: J. Biol. Chem. **183**: 81, 1950.
7. Griffiths, M.: J. Biol. Chem. **184**: 289, 1950.

COLLECTION OF BLOOD

Representatives of the American Medical Association, American National Red Cross, American Association of Blood Banks and the American Hospital Association have been meeting to aid in the development of the best possible blood transfusion service for physicians, hospitals and patients who use the blood—in fact, in the interest of national unity throughout the country. After carefully considering the information available, these representatives declared that it seemed advisable to cooperate with the National Security Resources Board by, in time of peace, providing for free exchange of blood between the American National Red Cross Regional Blood Centers and blood banks operating under other auspices on a unit for unit basis whenever and wherever it is needed to serve to the best advantage the interest of the community. It seems advisable for such units to be the property of the recipient blood bank to be used in accordance with its usual policy of issuing blood. As a principle, the groups favor making surplus blood available to the American National Red Cross or other agencies processing blood for the purpose of converting it into derivatives for the benefit of the people. By "surplus blood" is meant all blood that is not required for use as whole blood, plasma or any other derivatives by the blood bank concerned.

In the event of a disaster or a national emergency, the American National Red Cross, the American Medical Association, the American Hospital Association and the American Association of Blood Banks favor in those communities not served by an American National Red Cross Regional Blood Center the establishment of such a center and/or the use of existing blood bank facilities to procure the necessary amount of blood. The method to be used should be determined in a manner which meets the approval of the county medical society and the local blood banks and hospitals. Furthermore, the operation of the local blood bank facilities for civilian need should not be interfered with by the emergency program so far as consistent with government regulations existing at that time.

There is definitely a need for the use of standardized equipment and methods for the procurement and dispensing of blood; this is imperative in a national emergency and desirable in time of peace. To insure minimum standards all blood banks cooperating in such a procurement program should meet the minimum standards of the National Institutes of Health.

CODE OF ETHICS AND RESTRAINT OF TRADE

In 1947 legal action was commenced in the Supreme Court of New York County, New York, by the owner of a commercial laboratory to enjoin the New York State Society of Pathologists from enforcing a section of its Code of Ethics which declared that "it shall be unethical for a pathologist to act as director, employee or consultant for a commercial laboratory" and to obtain other relief.[1] The plaintiff's complaint alleged that this proscription and provisions for its enforcement unlawfully interfered with and restrained the free exercise by him of his business, that is, that the society's action was an unlawful restraint of trade. Judgment has recently been rendered denying relief to the owner of the laboratory. In his decision the trial judge said: "There is not a scintilla of evidence that they (the society's Code of Ethics) were conceived to restrain competition, to create a monopoly or hinder or obstruct the plaintiff or others similarly situated. If the indirect effect of the adoption of the ethical regulation was to cause plaintiff some incidental inconvenience, embarrassment, restraints, or even pecuniary loss, these are consequences that could flow from acts conceived with the highest and most unselfish of professional motives. They do not constitute in and of themselves ground for the granting of the repressive equitable relief sought herein." It is not known whether an appeal from the decision of the trial court is to be taken. It should be noted that this decision is based on the failure of plaintiff to prove the society's bad faith or want of reasonable purpose in adopting and in enforcing ethical principles.

HYPERVITAMINOSIS A

The paucity of the reports on the occurrence of the syndrome of hypervitaminosis A, in the opinion of Fried and Grand,[1] is probably due to lack of recognition rather than to its actual incidence. Josephs[2] in 1944 reported one instance of hypervitaminosis A in man, Toomey and Morissette[3] in another in 1947 and Rothman and Leon[4] in 2 more. Fried and Grand report the occurrence of hypervitaminosis A in an infant 16 months old and in another 2 years old. Both presented symptoms and characteristic roentgenographic bone changes, elevated vitamin A levels in the blood serum, a history of excessive intake of vitamin A over a prolonged period and a gradual complete recovery after withdrawal cf vitamin A. Clinically, the syndrome is characterized by anorexia, loss of weight, irritability, low grade fever, pruriginous rash, sparseness of hair, hepatomegaly and tenderness over the long bones. The storage of vitamin A and the regulation of its blood level are functions of the liver. Because of the capacity of the liver to store enormous amounts of the vitamin, Fried and Grand believe that the syndrome is caused by hepatic dysfunction rather than by supersaturation of the liver with the vitamin. Curves for vitamin A absorption in both of their patients demonstrated the existence of hepatic dysfunction. Awareness of the syndrome should lead to its more frequent recognition and to moderation in the employment of foods containing vitamin A in the diet of infants and young children.

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1. Rockmore v. Fein, et al, Supreme Court of New York County, New York (April 12, 1950).

1. Fried, C. T., and Grand, M. J. H.: Hypervitaminosis A, Am. J. Dis. Child. **79**: 475 (March) 1950.

2. Josephs, H. W.: Hypervitaminosis A and Carotenemia, Am. J. Dis. Child. **67**: 33 (Jan.) 1944.

3. Toomey, J. A., and Morissette, R. A.: Hypervitaminosis A, Am. J. Dis. Child. **73**: 473 (April) 1947.

4. Rothman, P. E., and Leon, E. E.: Hypervitaminosis A, Radiology **51**: 368 (Sept.) 1948.

WASHINGTON NEWS

(From the American Medical Association Washington Office)

Medical Reserves

The Army's announcement that it was calling individual medical reserves came while interest was still centered on Capitol Hill, where one Senator and half a dozen House members had introduced bills for the draft of former ASTP and V-12 students.

At the time the Army acted, no hearings had been held or scheduled on these bills. Furthermore, only one bill, that by Senator Chan Gurney (Republican, South Dakota), had been introduced by an Armed Service Committee member. Generally, emergency legislation is handled as a "committee bill," advanced with the backing of the full committee.

However, an Army spokesman said no legislative action could have altered the decision to send immediate orders to some "unorganized" reserves, who make up the great bulk of medical reserve officers. The spokesman said it would take several months for the draft-doctor bills actually to produce medical officers, ready for duty. To fill out the ranks with the required 734 physicians, a new system of selecting reserves was devised. The plan operates thus:

1. Each army command in Continental United States is under orders to supply a certain quota of medical reserves to report for duty by October 1. The quotas were arrived at by consideration of the "physician density" of each command, and apportionment of calls so as to take relatively few physicians from areas where the supply of physicians already is low. The equity and wisdom of this procedure is readily apparent, but it will also result in a heavy call on reserves in areas where reserve membership is low in proportion to general population.

2. An attempt also has been made to order up specialists on a geographic-population basis. Here again, while the method probably is as good as could be devised, the system will not work in the case of certain specialists—plastic surgeons, for example—where demand is out of all relation to supply.

3. Army commanders have been ordered to "make every effort" to enlist cooperation of medical societies in making their selections and to obtain the advice of senior medical reserves "wherever feasible." They are also ordered not to call up men from internships, residencies or full time postgraduate courses. However, the commanding generals may use their own judgment regarding reserves engaged in research of an essential nature or those practicing in doctor-scarce areas.

At the time it announced this action, the Army cleared up a point that might have been retarding its campaign for volunteers. Under a new ruling, all reserves going on active duty—voluntarily or involuntarily—keep the rank they held while inactive. Previously, they dropped back to the highest grade held on active duty, which often meant sacrificing one or two grades.

The Army also is reminding medical reserves that volunteering means $100 extra in pay for each month on active duty. This bonus is not allowed for men called on mandatory orders.

Bills for Drafting Physicians

Under provisions of the first doctor-draft bill introduced in the Senate, the ratio of physicians to total troop strength would be limited to four per 1,000. This is slightly higher than the ratio in effect when fighting started in Korea but is still appreciably less than ratios recommended by various ranking medical officers of the three services.

This bill (S. 4029) was introduced by Senator Chan Gurney (Republican, South Dakota) and is the first to be offered by a member of either Armed Services Committee. Senator Gurney is ranking minority member of the Senate committee.

The bill lists priorities for drafting of physicians, then states, ". . . during the life of this Act there shall be in the Armed Forces a ratio to total active strength of not to exceed four doctors of medicine and two dentists per 1,000 men. The Secretary of Defense is authorized to make allocations to the three military departments of numbers of doctors of medicine and dentists who may be on active duty, within the total ratios authorized."

Thus, the Secretary could allocate to the Navy, a ratio in excess of four per thousand of Navy strength and keep within limitations by making smaller allocations to the other two services. It should be noted also that this bill would not prevent the services, or the Defense Department, from employing civilian contract doctors for use in military hospitals.

Like most doctor-draft bills previously introduced in the House, Senator Gurney's bill provides for a National Specialist Category Advisory Board to "advise the National Selective Service System and coordinate the work of local draft board volunteer advisory committees with respect to the selection . . . of persons" for induction.

Under this bill, the first doctors to be called would be former ASTP and V-12 students who had served little or no time on active duty as medical officers. Next priority would be men who had served only limited periods of time in any branch of service.

National Medical Advisory Board

First suggestions for a National Medical Advisory Board were made by Representative John B. Saylor (Republican, Pennsylvania) and Carl Elliott (Democrat, Pennsylvania). It is Mr. Saylor's second bill on this subject. Their bills, like other doctor-draft bills, are aimed at bringing into active service former ASTP and V-12 students and others who have had little or no active duty. H. R. 9327, introduced by Mr. Saylor, and H. R. 9358, introduced by Mr. Elliott, are similar in many general respects, but differ greatly in detail. Both, however, would (1) authorize creation of a national board, to be composed of physicians and dentists, and of local committees similarly composed, to work with Selective Service boards, (2) exempt medical reserves from service under this bill but would require their registration unless they were on active duty, (3) be effective for only two years, and (4) require doctors inducted under its provisions to remain in the reserves for six years after release from active duty.

Medical Students and Selective Service

Despite some confusion over the matter, medical students are not affected by the most recent National Selective Service memorandum on the subject of college student deferment. This memorandum advises local draft boards that they may consider a registrant for deferment when the following conditions exist: 1. He has completed at least one academic year of college. 2. His scholarship placed him in the upper half of his class in the last full year completed. 3. The board is satisfied that he had "fully intended prior to Aug. 1, 1950, to enroll. . . ." However, exempted from application of the memorandum are "students of healing arts. . . ." Their situation is covered by an earlier communication to the boards, under which the boards may, at their own discretion, defer medical students if the boards are satisfied that their continuance in school would be in the national interest.

Women Physicians

A second day of committee hearings has failed to bring the Army, Air Force and Navy together on a uniform policy for commissioning and utilizing women physicians. Discussion is centering around H. R. 4384, an Army-Air Force bill providing equal treatment for male and female physicians. At the end of the second day of disagreement, Senator Lester Hunt (Democrat, Wyoming) told the witnesses: "Your group has confused me again. We thought that there would be an agreement between the three branches. However, even though we have read a letter from Secretary Johnson stating that he

favored this bill, the Navy comes here and states that they are not in favor of it—this is disappointing." Committee questioning brought out that Army and Air Force are in urgent need of more physicians. When the Navy witness was asked, "Don't you need physicians now?" he replied: "No, we have been ordering to active duty reserve officers. As long as we have that pool we cannot say that we have a shortage of physicians. . . . All women come in under the WAVE law, so they come in with their eyes open. Some of them feel they have better protection than do the line officers, because they do not compete with the line officers."

National Security Resources Board

A more important role may be decided on for the National Security Resources Board. This is the top federal organization concerned with civil defense and national resources, yet it has authority only to advise the President. Some Washington observers believe that operational power in this field must be granted to one single federal agency and that elevating NSRB is a logical development.

In view of this situation, new significance attaches to NSRB's action in creating a Health Resources Office at the highest level of NSRB. The director will be Dr. Norvin C. Kiefer, who has administered the now defunct Health Resources Division, which formerly operated on a lower level with fewer responsibilities. W. Stuart Symington, NSRB chairman, said the new office is charged with the vital task of planning for defense against atomic, biologic and chemical warfare. It will work closely with a newly formed Health Resources Advisory Committee, under the chairmanship of Dr. Howard A. Rusk.

In addition to planning a nationwide program to counteract special weapons attacks, Mr. Symington said Dr. Kiefer's office would deal with problems involving (1) mobilization, allocation and utilization of all personnel necessary for wartime health services in all health fields, (2) environmental sanitation services, including food and drink, rodent control, shelter and other sanitation, (3) veterinary medical services, including prevention of animal disease, (4) utilization of all health facilities, (5) collection and supply of all health equipment and supplies, including medicinals, biologic preparations and blood and blood derivatives, and (6) maintenance of essential teaching and research in the health fields.

While this is probably the broadest assignment ever given any one organization or individual in the health services field, Dr. Kiefer's group will continue in an advisory capacity only, in the absence of new legislation.

Atomic Bombing

An Atomic Energy Commission press conference has shed more light on the medical aspects of atomic bombing. The conference was called to discuss AEC's latest booklet, "Effects of Atomic Weapons," which was mentioned briefly in this column last week.

To a question on medical care of the people, an AEC spokesman said: "The principles of therapy developed during the last war will apply for the blast and burn injuries . . . the principles of treating shock and blast are just the same. For ionizing radiation we have no specific therapeutic treatment right now. . . ."

On radiation sickness, he said: "I think there is much that we can do about it. We don't have to sit back and say that 60,000 people are going to die because a bomb goes off, because that is not the way to look at it."

When asked if there was anything the individual could do when he knows he has been exposed to ionizing radiation, another spokesman replied, "There is nothing to do, and there is no problem. The biggest problem is what you can do with burns . . . and fractures. If an individual can stand up after the bomb goes off and look around and comment, 'This place is really beat up,' he is perfectly correct and he has a pretty good chance of surviving, something like a 90 per cent chance of surviving. . . ."

Asked about preventive shots against radiation, he answered, "It might be possible, but I doubt it. I would rather trust the treatment than a shot." Another spokesman added, that "with gamma radiation the primary thing is the mass of material that you can put between you and the source."

In discussing new technics in treatment of radiation, reporters were told, "In general, we can treat the symptoms, and of course the antibiotics have helped us an awful lot. . . ."

Question: "Do you have any substance as yet which treats the damage done to the cells themselves by radiation?"

Answer: "No, we have nothing specific against the exact invasion process. We still depend on the human body to recover of its own accord."

While most of the discussion on the medical aspects of the bomb centered on treatment and effects of radiation injuries, spokesmen emphasized that fractures, burns and shock demand treatment first and that, if a person suffered no injury other than radiation and survives, he can go for some time without treatment.

After some discussion of the tactical value of the atomic bomb against troops, one AEC spokesman emphasized that "it is safer in the Army than as a citizen at home."

Notes on Emergency

County medical societies are advised to obtain the Civil Aeronautics Administration list of 350 available ambulance planes. The list gives the planes' passenger capacity and equipment and day and night telephone numbers of private owners. . . . Army and Air Force nurse requirements at this date are being filled by volunteers, but the Navy began mandatory calls on reserves several weeks ago. The Army needs 750 nurses and the Air Force about 600; the Navy has not announced its needs. Army inquiries total about 15 a day, half requesting active duty. . . . The Navy cannot agree with the Army on the role of women physicians but has assigned one, Lieut. Comdr. Bernice R. Walters, to duty aboard a ship. The first woman shipboard physician is on the *USS Consolation,* headed for the Far East. . . . Dr. Joseph M. Pisani, New York, is the new executive director of the Committee on Medical Sciences of the Defense Department's Research Development Board.

Miscellany

A Department of Labor list, approved by the military, places doctors among those whose jobs are essential to civilian welfare. This is a guide, but advisory only, to military services in deferring reserve officers; the services themselves have last word on who is called up and when. . . . The Red Cross is directing research into methods of separating and preserving blood components, under an Atomic Energy Commission contract. . . . VA, describing the trained manpower reservoir built up under the GI bill, says that there are now more than 40,000 students studying medicine and related subjects. . . . FSA announces proposed minimum standards for all bread, a product of nine years' study and hearings. It limits the use of oxidizing agents, requires labels to list optional ingredients used and sets standards for enriched bread. Bakers and others have 30 days to file exceptions. . . . A new law (P. L. 673) gives the President authority to delegate many responsibilities, to save his time for major over-all direction. . . . Addressing planners for National Employ the Physically Handicapped Week (scheduled for fall) Mr. Truman said, "At a time like this it is essential that our country use all productive resources . . . the physically handicapped can and should be employed" . . . Senate committee amendments have taken the teeth out of H. R. 5965, which originally would have required the President to authorize the addition of 16,000 VA hospital beds. If the House agrees to this, the President and the VA will have almost complete freedom of action; they will be able to build none or all as they see fit. . . . House-Senate disagreements sent S. 3959 to conference; this spells out steps by which surplus government property may be distributed to medical and educational institutions. . . . Miss Louise M. Noble has been named chief of field services for the Children's Bureau. About a quarter of a million children are receiving care under the welfare program of the field services.

ORGANIZATION SECTION

MEDICAL CARE IN ENGLAND UNDER THE NATIONAL HEALTH SERVICE

Report to the Board of Trustees of the American Medical Association

WALTER B. MARTIN, M.D.
Norfolk, Va.
GROVER C. PENBERTHY, M.D.
Detroit
HEYWORTH N. SANFORD, M.D.
Chicago
ULRICH R. BRYNER, M.D.
Salt Lake City
and
CARL M. PETERSON, M.D.
Chicago

MISSION

On July 5, 1948, "The Appointed Day," [1] the National Health Service Act of 1946 went into effect in England, Scotland and Wales. This had been preceded by a long period of controversy between the organized medical profession in England and the Ministry of Health. The course of this discussion was followed with much interest in the United States, and it was with some surprise that we learned of the collapse of the opposition in the late spring of 1948. The detailed provisions of the Act were not well known in America, nor were the reasons for its rather sudden acceptance by the major portion of the English medical profession.

As the experiment progressed, much information, often conflicting in nature, began to filter back to the United States. It seemed desirable, therefore, that we should profit by the experience of England under the Act and should be possessed of as accurate a picture as possible of developments in England during the eighteen months' operation of the Act.

The Board of Trustees of the American Medical Association, therefore, appointed a group of five members of the Association, qualified in separate branches of medicine, and directed them to spend a period of not less than six weeks in England, Wales and Scotland and to inquire into the present workings of the National Health Act, particularly, as to its present effect on the quality of medical care and what, in their judgment, would be its probable future effect.

PROCEDURE

In accordance with the directive, the group appointed arrived in London on January 4, and during a period of six weeks endeavored to fulfil its mission. It soon became apparent that a statistical approach to the problem was impossible. The financial and statistical year extends from April 1 to March 31 of the following year, so that the first complete year would not have ended until March 31, 1950. Comparison may then be made of that year and the year of 1947, the last complete twelve month period prior to the effective date of the Act. The committee felt that the only possible method of evaluating the situation was by multiple observations, in different areas, of the actual working of the plan—in the home, the practitioners' offices, the outpatient departments of hospitals and in hospitals of different sizes and types. In addition, general practitioners, specialists, hospital superintendents, public health directors, members of regional boards, executive committees and local health authorities were interviewed singly and in groups. Everyone from the Ministry to the local executive committee within and without the service were most cooperative and helpful. We were given every opportunity to make as full observations of all parts of the working of the Act as time permitted. The officials of the British Medical Association, of the Scottish and Welsh branches and other divisions of the British Medical Association also extended us every facility.

The appendix lists the acts under which certification is required.

1. The date set by the Minister of Health for activating the National Health Act of 1946.

BACKGROUND OF THE ACT

It is evident that, while the Act effected a sudden and radical change in medical practice in England, conditions favorable for its enactment had been developing for many years. These conditions were dissimilar to the situation that prevails in the United States. While the medical systems of the two countries have much in common, they diverge at many points.

The system of hospitals in England began during the monastic period and continued as a place of refuge for the destitute sick, until the seizure of the monasteries under Henry VIII. When reopened, they still retained their original purpose. These hospitals, and other voluntary hospitals since developed, continue to serve predominantly the poor. Only in comparatively recent years has provision for private patients been developed, in connection with the large general hospitals. On the effective date of the Act it is probable that not more than 5 per cent of the beds in the teaching and other large general hospitals were for private patients. These hospitals were supported largely by permanent endowments, gifts and money derived from contributory plans. The patients admitted to their wards were usually restricted to certain low income levels and paid to the hospital for their care only such nominal sums as they could individually afford. Their professional care was provided without cost by the consultants who staffed these hospitals. The patients above this income group engaged private practitioners, and, when in need of hospital services, were cared for either in the rather limited private pavilions of general hospitals or, more usually, in one of the numerous nursing homes.

The second group of hospitals had grown up under the old Poor Law. These were the municipal or borough hospitals and were almost exclusively devoted to the care of the poor. They provided for the chronically ill, mental cases, contagious diseases, tuberculosis and general hospital cases. These hospitals varied considerably in efficiency, but under the influence of progressive local public health authorities many of them had reached a high degree of professional excellence. The control of the contagious disease hospitals and the tuberculosis sanatoriums naturally became the special responsibility of the Public Health Service. This service was thus able to integrate the entire care of the tuberculosis patient, including prevention, home treatment and presanatorium, sanatorium and postsanatorium care.

In addition to the large hospitals, there were scattered throughout the smaller cities and towns the so-called cottage hospitals. These as a rule were not capable of giving complete hospital and professional care but served a useful purpose, as the less complicated medical and surgical problems could be cared for locally and often by the patient's own family physician. Some of these were developed under the Local Health Authorities, and others were private in character.

The financial support of the municipal or borough hospitals came partly from subsidy from the central government. The central government's contribution was 50 per cent of the total amount, plus an additional lump contribution, in certain less economically secure areas. It should be emphasized that there had been pronounced and progressive improvement in the quality of service rendered by this group of hospitals. The effect of the war, which continued into the postwar period, was to bring hospital construction and improvements almost to a standstill. The Queen Elizabeth Hospital in Birmingham, which opened in 1939, and one large hospital in London which opened in 1941 were the last major units added to the hospital system.

The great central hospitals in London were evacuated during the period of bombing, but their staffs were maintained on a standby basis for the care of casualties, both military and civilian. The government financed this procedure together with a per diem payment for occupancy. The burden of the war, together with the high rate of taxation, had served to decrease income from endowment and to dry up future endowments and other sources of income for the voluntary hospitals. They

were thus faced with a serious financial problem, both from a standpoint of replacement of war losses, including needed improvements, and also of meeting their ordinary operating expenses. Operating expenses had increased as in America. The demand for services had also mounted as sources of revenue had diminished. Therefore, government subsidy appeared to be the only answer. They were, of course, met with the old familiar argument, that what government finances it must control.

It is thus seen that two separate hospital systems had grown up side by side, namely, voluntary hospitals and the locally controlled municipal or borough hospitals. These two systems were not correlated or integrated. The British Medical Association had long advocated some form of correlation, preferably on a regional basis, so as to establish a more coordinated system of hospitals.[2] In Scotland similarly the grouping of hospitals with the hospital of a medical school as a center was advocated in 1944.

Another factor in the decay of medical practice in England was the National Insurance Plan, which has been in operation since 1912. This provided general practice care for all workers, a very considerable segment of the population. The number of persons affected by the Act of 1912 had been greatly increased, and more than 80 per cent of the approximately 21,000 general practitioners had panels of varying sizes. These practitioners had become accustomed to that type of practice, and the transition from a panel to a list under the new Act was effected without shock. Many of the shortcomings in medical practice noted under the National Health Service Act were present under the old panel system. It is true that there were many general practitioners without panels, or whose panels were so small that they did not seriously affect the practitioners' attitude toward medicine, but some of those whose panels served as a principal source of income acquired a somewhat different attitude. When the government service was extended to include dependents, the panels expanded to lists and the panel doctors fell heir to the major portion of general practice.

Long before the Act, the English people had moved far in providing certain ancillary medical services. The Local Health Authority, through the Medical Officer of Health, was furnishing a variety of these services, in addition to that provided by the Department of Education in the schools.

Public health organizations, with particular attention to environmental sanitation, were established in 1831 to meet the peril of a cholera epidemic. In 1866 certain special hospitals, notably those for tuberculosis, contagious diseases and mental diseases, came under the local medical health authorities. After the Boer War in 1899, attention was focused on the poor physical condition of the recruits at that time. A commission was appointed to study the causes of this, and in 1908 a school health system was established under the Department of Education. This gradually extended to include complete dental and medical care for all school children. At this point the general practitioner began to lose touch with the problem of the family as a whole.

In 1930 the old Poor Law was abolished and the Poor Law Hospitals were transferred to the Local Health Authorities. There are in England 146 separate health authorities operating in 83 towns and 63 counties. The population of these units varies from 15,000 to 4½ million. In addition to other activities in connection with environmental sanitation and the operation of local hospitals, the Local Health Authority provided a number of services of a more personal nature—domiciliary midwife services, prenatal care, child welfare centers, home nursing, vaccination and immunization, mother guidance or mother craft, health visiting, home help services and ambulance services. It must be understood that these services were either required or were permissive before the Act. It will be thus seen that a large amount of medical social service had already been provided for the British people, and they had been trained to look to the government for help in any emergency rather than to rely on their own efforts.

Into this situation in 1942 came the report of Sir William Beveridge, entitled "Social Insurance and Allied Services."[3] This closely reasoned and persuasive document exerted a considerable influence on social thinking. It is probable that few persons read in detail the nearly 300 pages of fine print in this report; most were persuaded by headlines or reviews or a hurried perusal of some of the main paragraphs. His reasoning was based on three assumptions, which he states are necessary for the success of any satisfactory scheme of social security. We are concerned primarily with the second assumption, "comprehensive health and rehabilitation service for the prevention and cure of disease and restoration of capacity to work available to all members of the community." This report is mentioned at this point because it decidedly influenced the thinking of men of both the socialist and conservative groups and eventuated in a statement by the coalition government (the so-called White Paper) giving its blessing to some type of government-financed comprehensive medical care.

In 1930[4] and again in 1938[2] the British Medical Association issued an official statement in reference to their opinion on the setting up of a more comprehensive health service and the coordination of the existing hospital services. The National Health Insurance Plan was praised wholeheartedly, and it was strongly urged that it be extended to include the dependents of workers. This and other factors are brought out here to indicate that progressive changes had been taking place in British medicine and that these had led up to the enactment of legislation providing for a complete national health service in 1946. The present situation cannot be appreciated without some understanding of this historical background.

The bill as passed by the Socialist party in 1946 contained two important provisions not included in the recommendation of the coalition government or of the British Medical Association. These pertained to the seizure of hospitals, both voluntary and municipal, and made it unlawful to sell or buy a medical practice. This last, as will be brought out later, was a principal factor in forcing the general practice segment of the profession to accept the new law.

POLICY OF THE BRITISH MEDICAL ASSOCIATION

The policy pursued and actions taken by the British Medical Association, prior to the activation of the health insurance act, deserve some comment. A pamphlet was issued by the association, after the plan went into effect, explaining its position.[5] Over a period of many years the British Medical Association, through its Council and through special committees, made careful studies of the problem of medical care and in 1930[4] and again in 1938[2] published rather comprehensive statements, in which they recommended extension of insurance to the dependents of workers, including dental and ophthalmic benefits and consultant service.

At this time and later the British Medical Association urged the integration of the hospitals into one system, preferably on a regional basis and centered around teaching hospitals. In 1942 the Medical Planning Commission of the British Medical Association made its recommendations.[6] In general, these were along the lines of previous reports but were enlarged on and given added emphasis. After this, interest in Parliament was stirred by the Beveridge Report, and in February 1944 the Coalition Government issued a White Paper, which contained its proposals for a National Health Service. The proposals before Parliament went further than previously advocated by the medical profession, especially in reference to making the health program comprehensive. Discussions, however, were going on between the British Medical Association and the Ministry of Health when the Socialist Party gained control of the government in 1945. The present act was introduced into Parliament and passed without previous consultation by the Socialists with the medical profession.

The first plebiscite was in June 1947 and showed a majority of 54 per cent against the Act. This led the ministry to agree to discussions, and these went on until November of that year. These discussions were barren of results, as the Ministry rejected all suggested changes.

2. A General Medical Service for the Nation, London, British Medical Association House, November 1938.
3. Beveridge, W.: Social Insurance and Allied Services, London, His Majesty's Stationery Office, 1942.
4. The British Medical Association's Proposals for a General Medical Service for the Nations, London, British Medical Association House, August 1930.
5. The Medical Revolution in Great Britain, London, British Medical Association House, 1949.
6. Draft Interim Report, London, British Medical Association House, 1942.

The second plebiscite, in February 1948, showed an overwhelming majority against the Act; 38,534 against and 4,479 for. Negotiations were resumed two months later, and certain concessions were made by the Ministry, notably in reference to reducing the power of the Medical Practice Committee, assurance that a basic salary would not be set up, elimination of nursing homes from the hospital seizure and a promise to continue private pay beds and to allow specialists in hospitals to choose to work part or full time. It is significant, however, that the power of the Minister was not materially diminished. Apparently the seriousness of this, particularly his control over funds and authority to make regulations having the effect of law, was not fully appreciated, as it was the last of the objections to the bill noted by the British Medical Association. The concessions made, however, had some effect on medical opinion but do not altogether explain the change in sentiment that occurred before April, when the third plebiscite was held. In a 77 per cent return, 64 per cent were against accepting service under the Act and 36 per cent for acceptance. This percentage of return was smaller and reflected a considerable amount of indecision on the part of many doctors. The House of Representatives of the British Medical Association met on May 28, and in spite of an almost two-thirds vote against acceptance in April, voted to recommend that the profession sign contracts for service. This date may be significant. The Minister had ruled that only those general practitioners who signed before the effective date of the Act would benefit by reimbursement from the fund set up for payment of the value of their practice. Time was short, and the threat to the security of many men and their families was very real. Just what law of ethics would indicate that a man who joined on July 4 was entitled to payment but was not so entitled if he joined on July 6 is not entirely clear. There were a number of undecided points between the profession and the Ministry that were left for future adjustment, and some of these continued to disturb the relationship between the profession and the Ministry.

Since the Act went into effect the doctors have on the whole accepted its provisions and have attempted to make it work. If it fails there will be no reflection on the good faith of the medical profession.

THE ACT

The Promise.—The National Health Service Act[7] as made effective on July 5, 1948, provided for hospital and specialist service of all kinds, including mental hospitals, sanatoriums, maternity accommodations, treatment during convalescence, medical rehabilitation and other institutional treatment. It covered inpatient and outpatient services, including clinics and dispensaries operated as part of any specialist service. The advice and services of specialists of all kinds were also to be made available when necessary at health centers and in the patients' homes. It provided general personal health care by doctors and dentists of the patient's choice. The general practitioners' services were to be available both from new publicly equipped health centers and from the practitioners' own surgeries. Various supplementary services were provided including midwifery, maternity and child welfare, health visiting, home nursing, a priority dental service for children and expectant or nursing mothers, domestic help where needed on health grounds, vaccination and immunization against infectious diseases, additional special care and after-care in cases of illness, ambulance service, blood transfusion and laboratory services. It was to be integrated with the special school health service already provided for in the Education Act of 1944. It also provided spectacles, dentures and other appliances, together with all drugs and medicines at hospitals, health centers, clinics, pharmacists' shops and elsewhere as needed. All of this service or any part of it was to be available to anyone in England and Wales. There was no limitation imposed on the basis of economic status, age, sex, place of residence, employment or insurance qualification. While a small part—about 6 pence of the over-all social insurance contribution—was to be set aside and assigned to the Health Service, the service was in no way dependent on this contribution or on an insurance feature in any way.

7. National Health Service Act of 1946.

How Implemented.—The act placed on the Minister of Health the responsibility for promoting this all-embracing health service. It is activated through three main channels:

1. The hospitals and specialist service, administered by the Regional Hospital Board, together with a blood transfusion service and bacteriologic laboratories for the control of infectious disease, directly under the Minister.

2. The local health service, administered by the Local Health Authority. This includes a variety of special services in clinics and in homes, similar to the program previously carried out under the local councils.

3. The general practice service, which provides the services of the family doctor, the dentist, the pharmacist and the ophthalmologist and is administered by local executive committees directly responsible to the Minister.

The functions of the Minister are discharged through a number of councils and committees, at the level of the Ministry; through Regional Hospital Boards, or in the case of teaching hospitals through a Board of Governors for each hospital; through Local Health Authorities, and through Local Executive Committees. The striking point about this system is that, while administration has been decentralized and, incidentally, made cumbersome, power and the control of finances has not. At the Ministry level is the Central Health Service Council, hereafter called the Central Council. It is composed of 41 members and acts in an advisory capacity to the Minister. It has as ex-officio members the Presidents of the three Royal Colleges, the President of the General Medical Council, the Chairman of the Council of the British Medical Association, and the Chairman of the Council of the Society of the British Medical Officers of Health. There are in addition, 35 members appointed by the Minister after consultation with such organizations as he may consider representative of the interest concerned. There are in this group 15 practitioners of medicine, two of these shall be selected for their knowledge of mental diseases, five persons with experience in hospital management, three persons experienced in local government, three dental practitioners, two persons experienced in mental health service, two registered nurses, two pharmacists and one certified midwife. The Minister is empowered to appoint standing committees consisting partly, but not altogether, of members of the Central Council, such as medical, maternity, midwifery, cancer, radiotherapy, mental health, tuberculosis, ophthalmology, pharmacy and nursing. The Central Council itself may also appoint additional subcommittees, and the advisory committees may appoint subcommittees. The standing committees may advise the Minister directly, provided that they inform the Central Council. This Council may consider matters referred to it by the Minister or may take up matters on its own initiative. It is required to make an annual report to the Minister on its work and on that of the standing committees. The Minister is required to publish this report and present it to the Parliament, unless he feels that it contains matters that in the public interest should not be published. It is evident that the Central Council, while composed of very eminent men and women, has little power and acts only in an advisory capacity. The Minister does not have to seek the advice of the Council; if he does seek it, he does not have to follow it. Its principal source of influence is through the publication of its annual report. The Minister can change the composition of the Central Council at will.

The Scottish Health Service Council consists of 35 members, appointed by the Secretary of State for Scotland after suitable consultation. It has no ex-officio members and is made up of 18 medical practitioners, four persons experienced in hospital management, five experienced in local government, three dental practitioners, two registered nurses and one certified midwife.

There are, in addition, several other advisory bodies at the level of the Ministry:

1. A Medical Distribution Committee, which allots to each local executive committee its share of the total sum set aside for the payment of the general practitioners. This committee also handles the general practitioners' mileage fund, amounting to approximately two million pounds.

2. The Medical Practice Committee, which in consultation with the local executive committee and the local medical prac-

tice committee, determines the question of doctors' locations, with particular reference to decreasing the number of doctors in over-doctored areas, and the encouraging of doctors to enter areas where they are needed. This committee consists of a medical chairman with eight other members, six of whom are doctors.

3. A Practice Compensation Committee of five, three of whom are doctors, may advise the Minister on all claims for compensation which may be referred to them.

4. The Tribunal is a semijudicial body and final board of appeals, except to the Minister, in matters relating to professional conduct or complaints lodged against a doctor, pharmacist or dentist. Cases come to the Tribunal from the local service committee through the local executive committee. The Tribunal is made up of three members. The chairman is a solicitor, appointed by the Lord Chancellor; a second is a layman appointed by the Minister and the third is one of a panel of six doctors selected for their particular professional qualifications to judge the case at point. This panel is selected by the Minister after consultation with what he considers appropriate organizations. This body has the power to reprimand, fine or finally remove a doctor's name from the list of approved practitioners. This last penalty amounts to exile or starvation, since a list doctor could not hope to build up a private practice in England today.

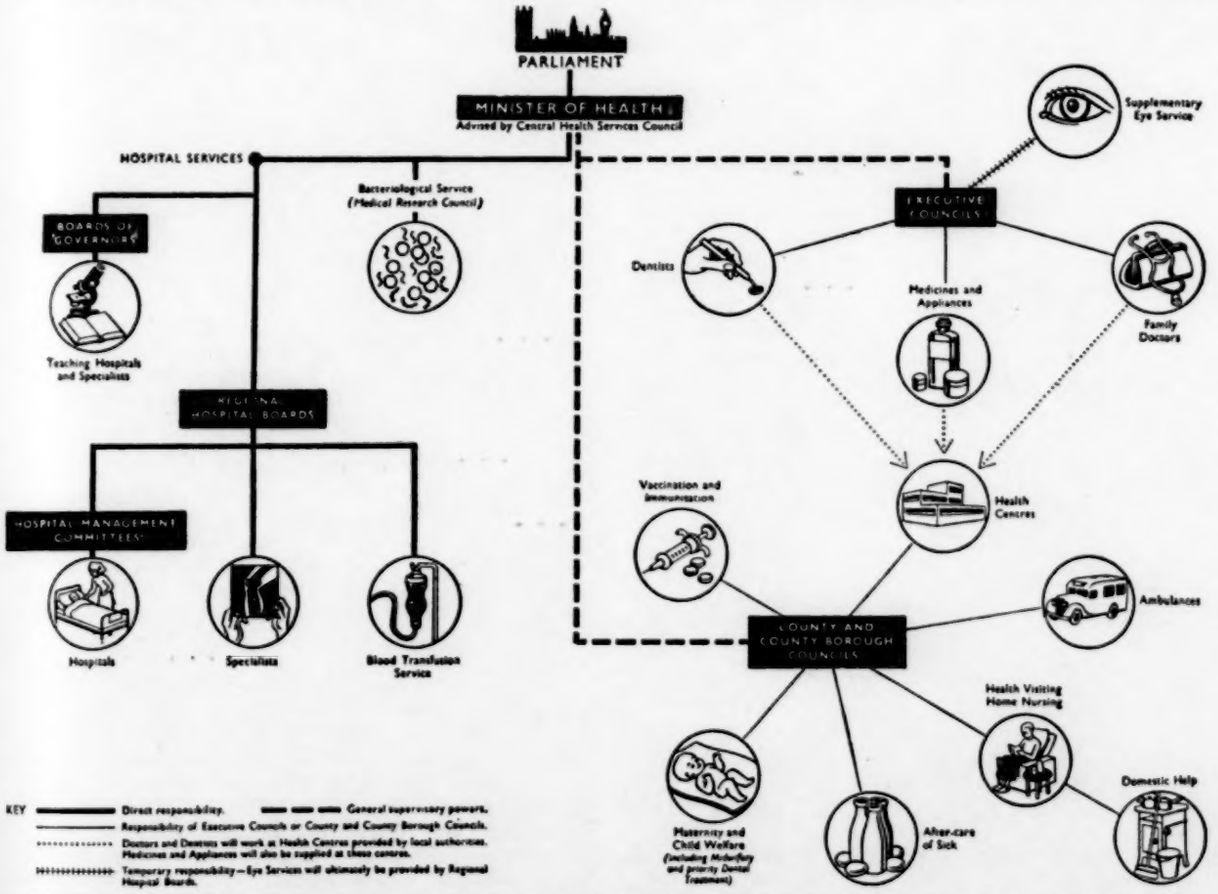

Diagram giving a broad view of the organization of the National Health Service, with omission or simplifications of some of the details.

HOSPITAL AND SPECIALIST SERVICES

Organization.—The 3,426 hospitals and clinics taken over by the Ministry have been placed for administrative purposes under 14 regional boards, except for the teaching hospitals in England and Wales. In Scotland all hospitals are under these boards. In England and Wales each teaching hospital has its own Board of Governors, directly responsible to the Minister. The regions were planned so that there would be at least one medical school with teaching hospitals in each. Since there are 22 medical schools in England and Wales, this, of course, means that in certain of the 14 regions, there is more than one medical school. In Scotland, with four medical schools, the natural division found a medical school in each of four regions. The fifth region, in northern Scotland is centered on Inverness, with an excellent General Hospital.

The memberships of these boards vary from 22 to 32; all are appointed by the Minister. He receives nominations or recommendations from groups that he considers properly interested in hospital management. Slightly less than a third of the membership of the 14 boards are doctors of medicine. When first organized, the Minister appointed the chairman of each board, but now the chairman is selected by the board. These boards have two principal functions to perform. They are charged with the duty of administering the hospitals in their area and of organizing and providing specialist services.

The Hospitals.—For the purpose of administration, the hospitals under the Regional Hospital Boards are formed into 376 hospital groups, each under a Hospital Management Committee. To these management committees is delegated the immediate administration of the hospitals through a lay or professional superintendent. This grouping of the hospitals has for its purpose the bringing together of hospitals rendering different types of service, so as to provide a unit which in general would be self containing as far as being able to furnish almost every type of service. Inside these groups, and often in the separate hospitals, are professional committees representing different departments that deal with the Hospital Management Committee. This rather complicated system has thrown a heavy burden of committee duty on many doctors, and especially on some, as many of these committees are interlocking. This type of organization does not lend itself to speed. The recommendation of a professional committee in a hospital will go to the Hospital Management Committee, through the hospital administrator, then to the management committee for the group and then to the Regional Hospital Board. The reply will travel back along the same devious route, so that a debate on a particular point may extend over many months. This feature was commented on by almost every hospital administrator with

whom we came in contact. Funds allotted to each Regional Hospital Board are in turn divided among the several hospital groups and individual hospitals, according to the judgment of the board and on the basis of estimates submitted by each institution. In the reverse, each hospital or group of hospitals submits an estimate of anticipated expenditures to the Regional Hospital Board. These estimates are acted on by the board and if approved are consolidated and sent to the Minister as an estimate for the region. This estimate may be accepted by the Minister or sent back to the regional boards for revision.

The Specialists.—The Regional Hospital Boards are also responsible for providing specialists services in the hospitals, outpatient department, clinics and the home and appoint all specialists, either full time or part time.

The resident house staffs are appointed by the Hospital Management Committees but are paid on a scale set by the Minister. This scale begins at 350 pounds per annum for an intern and extends up through the various grades to as high as 1,300 pounds for a senior registrar.

When the Act went into effect final agreement had not been reached on payment of service for the specialists. In general, the specialists at that time serving in hospitals were appointed in the positions that they then held on a temporary basis. Permanent appointments have now been made according to the agreed scale of payments, arrived at after consideration of the subject by the Spens Committee.[8] All vacancies that occur now are advertised, and the applicants are considered by a suitable professional advisory committee, appointed by the board and reporting to the board. Consultants work and are paid on a so-called sessional basis. A session is three and a half hours, which includes the time in transit from home or office to the hospital and return. A full time consultant works eleven sessions a week and may not engage in private practice. He is paid on a scale beginning at 1,750 pounds if he is 32 years of age and increasing 125 pounds each year to a total of 2,750 pounds. At this point he is "frozen" for life unless he is selected for one of the special merit groups, of which there are three grades. The highest of these may include 4 per cent of all the specialists, and a member of this group receives an additional 2,500 pounds per year. A specialist in the second group, which comprises about 10 per cent of all specialists, receives an additional 1,500 pounds, and one in the third group (20 per cent) receives an additional 500 pounds per annum. It is possible, therefore, for a specialist to progress up through these several grades, until he receives a maximum of 5,250 pounds. If he is of unusual eminence, he may be appointed directly to the highest grade. A professional committee is now engaged in the thankless job of making these awards.

The part time specialist may elect to work for any number of sessions, not to exceed nine, and may engage in private practice. In addition, he may add to his income by taking home consultations at 4 guineas each, up to a total of 200 consultations in one year, or a total of 800 guineas. He is paid the appropriate fraction of the salary scale of the full time consultant and may share in the special distinction award of the full time consultants on the same fractional basis.

Finally the Boards of Governors and the Regional Hospital Boards are "required to perform these duties subject to and in accordance with any directions the Minister may give."[7] These come out at an average rate of about two per week and now fill three fairly large files.

It was generally felt that the provisions which gave a preferred financial position to the specialist constituted a potent factor in dividing the profession and in opening the way for the acceptance of the Act as a whole by the House of Representatives of the British Medical Association. The specialist, if he wins recognition as such, is given an assured income and rather limited hours of work. On full time he works only 38½ hours each week, including travel time to and from his place in the galley. The only thing that he has lost is freedom. He is as surely chained to his post as though he were bound by visible shackles. The high rate of pay provided for doctors in training courses leading to specialist rating has stimulated a rush into this field. The crowded conditions of the hospitals has created a need for larger house staffs, so at present there are in training, looking toward specialist degrees, many times the number of doctors needed for normal replacements. This means insecurity for those that now hold hospital appointments, since in a short while there will be a host of applicants crowding on their heels. These hospital appointments are made by the Regional Hospital Board, which in turn is appointed by the Minister, who can change the composition of the board at any time. To suggest that this makes for freedom of thought or independent action on the part of the specialist is to state an absurdity.

To further add to the confusion and conflict of interest the "golden apple" was thrown into the arena of the specialist. There were to be not only specialists but superspecialists. The three grades just mentioned were established with the possibility that 4 per cent of the specialists might receive 2,500 pounds in addition to the regular salary of a specialist. A commission is now engaged in selecting those to be so favored. It is difficult to imagine a plan better calculated to destroy the unity of the profession.

The maximum pay that a full time consultant can earn is based on eleven sessions of three and a half hours each per week. No matter how great the need or how willing the worker he cannot earn a single extra shilling by devoting more time to serving the long list of patients waiting at the door of the hospitals. Regardless of the effect of this plan in weakening the moral fiber of the physician, and destroying the age long concept of the profession as to its duty to labor diligently as long as there is suffering that needs to be relieved, the waste of medical talent is appalling. One wonders whether this plan was conceived in ignorance or with the cynical purpose of corrupting an ancient profession.

How Regulated.—On the "Appointed Day" the Minister took over ownership of nearly all of the country's hospitals, including both the voluntary and local health authority hospitals. The exceptions to this were a few hospitals under control of religious bodies and a small number that the Minister rejected for his own reasons. Under the term hospital there are included the large teaching and voluntary hospitals, the local hospitals, both of the general type, and the special types for tuberculosis, contagious disease, mental disease and mental deficiency. Also included were most of the cottage hospitals, but the private nursing homes were not seized. The Minister was given complete authority to organize a system of hospital care. The Act provides for a comprehensive program of hospital and specialist benefits for everyone in the community. The Minister's power extends further. He may make three kinds of hospital provision, namely, wards, semiprivate and private. He has the power to decide what use will be made of any hospital accommodation. He may convert the accommodation from private to public, or vice versa. Subject to accommodations being available, patients may make their own choice of the type of accommodations they desire. Hospital benefits, except in emergency, are usually provided on order of the general practitioner. He need not be a practitioner under contract with the government. There is nothing in the Act to restrict persons seeking hospital care to hospitals within the area of their residences, but each has the right to choose the particular hospital where he would like to be treated. He pays nothing for his hospital service or outpatient care, unless he occupies a private room without medical necessity. In this case he pays 2 guineas a week for this so-called amenity privilege. He may have his expenses in traveling to and from the hospital or the outpatient department paid, together with expenses of a traveling companion, if such companion is thought necessary. He may have free transportation by ambulance or sitting car, either to the hospital or to the outpatient department. He may be attended by a specialist at home if the practitioner recommends it. Neither the patient nor the general practitioner is given the right to choose any particular specialist either in or out of the hospital. It is the responsibility of the Board of Governors or the Hospital Management Committee to organize this domiciliary service. There is no provision in the Act for consideration of complaints by patients receiving hospital or specialist service as contrasted to the rather elaborate machinery set up for this purpose in the General Practice section.

Hospital Management Committee.—These committees are appointed by the Regional Hospital Boards and are charged

8. Report of the Inter-Departmental Committee on the Remuneration of Consultants and Specialists, London, His Majesty's Stationery Office.

with the immediate responsibility of operating the hospital or hospital group. In the case of large groups there may be such a committee for the group and separate ones for the larger hospitals in the group. Appointments to these committees are made on recommendations of the professional hospital staff, the local health authorities, the local executive committee, the local social service organization and the various consumer groups that are considered to have an interest in the hospital management. The Management Committee operates through a hospital administrator, who may be either a doctor or a layman. They are at all times subject to such regulations as may be issued by the Minister. These regulations are numerous and detailed. While there is an outward form of local control, they are under the direct supervision of the Regional Board and the not very remote control of the Minister of Health. In Scotland, this committee is called the Board of Management and includes, in addition to the aforementioned members, such persons as the Regional Hospital Board deem fit. In the case of teaching hospitals up to one fifth of the membership of the board may be nominated by the University.

Quality of Service.—Professional care in the hospitals is handicapped by the chronic overcrowding and the pressure of a long waiting list. Occupancy runs from 90 to 95 per cent. This has decreased the efficiency of the hospitals, and the turnover rate in general hospitals is rather slow. In general, the average patient stay is 16 to 20 days. At times this average is increased by the presence of patients with chronic disease who cannot be discharged for lack of facilities for domiciliary care. In one large hospital, with a waiting list of 7,000, there were 40 patients who had been in the hospital over 100 days. This is offset, however, by the fact that the number of emergency admissions is high. Crowded conditions do not lend themselves to the best clinical work, and the great load of the clinical laboratories and x-ray services has further tended to slow down the whole procedure. Individual specialists are carrying on in much the same way as before. The momentum of the old system has not been lost, and the quality of individual care that comes directly under the older men has not materially altered. The number of registrars in training has been increased, probably doubled, and more responsibility falls on these young men in training, so that there is naturally less time for their supervision. What this will mean in terms of quality later remains to be seen. There has not yet been time for the "new look" to appear, although one catches a glimpse from time to time. The large general hospitals are certainly not discharging their real function, taking care of the seriously ill and the problem cases. These are being crowded out by minor cases that should be filtered out in a general practitioner's office or in the outpatient department. There is no sign of abatement of the demand or of any provision for a better filter.

The Private Patient.—As previously stated only about 5 per cent of the hospital beds are private accommodations. The first call on these quite properly is for those who have need of them for medical reasons. The next priority is for the use of government patients who desire privacy and who are willing and able to pay the 2 guineas charged government patients for this service. If there are any left over, they are available for private patients. There is another limitation, however—all but 15 per cent of the private beds are so-called ceiling beds. Under this ruling a surgeon having a patient in a ceiling bed is limited in his charge to 75 pounds. This sum must also include the cost of any diagnostic procedures, such as clinical laboratory and roentgenographic, and must be shared with any other consultant associated in the case. The private patient occupying a single room pays the average per diem cost of the hospital plus 25 per cent. This has made these rooms so expensive that few patients can afford them, and, if they wish to be treated by a private physician, they must have recourse to a nursing home.

Operating Cost.—There has been a sharp rise in the per diem cost or in the weekly cost, as is usually calculated in England. This increase has been going on for the past 10 years and in part is due to the general rise in cost of living. Part of it is the result of a justifiable wage increase, particularly in the case of nurses. An additional item of cost has been the salary list for consultants and residence house staff. Prior to the Act, the consultant's services were given without charge and the rate of pay for the resident house staff was much lower. These factors, however, do not account for the total increase. Hospital administrators and other informed persons repeatedly refer to the great increase in the administrative and clerical staff. This has resulted from the "mountainous" addition in paper work and the exactions of repeated ministerial directives. Exact figures on the relative administrative costs before and since the Act were not obtained, but testimony to the effect that this increase is great is convincing. Administrators also repeatedly stressed the fact that before the Act considerable help came from voluntary organizations that aided in various ways in the work of the hospital. These voluntary assistants have largely disappeared. Endowments also, which in some hospitals were considerable and allowed the hospital to charge lower rates, have been absorbed by the government. An interesting comparison was obtained between general hospitals operating under the Act and one operated by an independent board. The weekly operating cost of the latter is about two-thirds that of similar type hospitals under government direction. Funds for operating each hospital are allotted by the Regional Hospital Boards on the basis of estimates submitted and funds available.

Future Financing.—Estimates of income and expenditures are submitted by Management Committees, Boards of Governors and Regional Hospital Boards for approval by the Minister. Regulations provide in detail for a uniform accounting system. The estimates may or may not be approved by the Minister and may be returned by him to the boards for revision. The budgets have to be approved in detail as to the amount of central administrative cost, the amount other than administrative and the amount for each hospital in the group separately. It is to be noted that wages comprise over 55 per cent of the total operating cost. It is also to be noted that, if the Minister disapproves of a budget and orders a cut, this cut cannot be applied to wages except on joint agreement between the Minister of Health and the Minister of Labor. Since the hospitals are entirely dependent on the government for support, any financial crisis in the government will reflect itself in hospital finances. It should be remembered that the health services receive nearly 90 per cent of their support from direct taxation. The administrators of the hospitals chafe under the restrictions placed around them in discharging their duties even in relatively minor details. Except in emergencies, they cannot expend more than 2 pounds without authorization from the Regional Board, nor can they take on an additional employee except as a replacement without such authorization.

Endowment.—In the case of teaching hospitals endowment funds passed to the new Board of Governors free of any trust agreements existing immediately before the transfer. They were given power to dispose of or transfer property. Endowment funds of the voluntary hospitals passed immediately into a central hospital endowment fund or pool. The authorities are required to secure as far as reasonable the use of these funds for the objective for which they were given. In Scotland the endowment of each voluntary hospital was transferred directly to the Secretary of State with the duty of reviewing all endowments and of making plans for their future management and distribution.

Further Acquisition of Hospitals.—Hospitals not transferred to the Minister on the appointed day or disclaimed by him cannot be acquired now except by purchase or gift.

Outpatient Department.—The general plan of operation of the outpatient department of hospitals has not been essentially changed since the Act went into effect. There has been a considerable increase in personnel, both clerical and professional, because of the great increase in patient load. The almoners have been entirely relieved of that portion of their duties that had to do with assessment of the patient's ability to pay and now devote their entire time to medical social service activities. There has been on the whole little expansion in facilities, nor is this possible without rather expensive structural changes. It should be remembered that this is a consultation service and that the staff is made up of consultants, with their assistants and registrars. The number of these teams has been increased, and in most of the departments visited full use was being made of all physical facilities. In spite of this, there are long waiting lists in every instance. While an effort is made to sort

out and care for those in urgent need, this is difficult to accomplish. In general, the patients are referred for consultations by a practitioner, either with a note or with a referral slip, and appointments are made. It has been necessary to operate by appointment only, and often appointments are deferred for several weeks. Even after appointments are met there are further long delays in securing reports on diagnostic laboratory and roentgenographic procedures. After the patients' studies are completed, a note outlining findings and giving advice as to treatment should go back to the general practitioner. As a result of the great pressure for appointments, the length of time allowed for each patient has been shortened in many instances. While this may be necessary, it does not tend to improve or even maintain the quality of work.

There are several complaints commonly made by the general practitioner in reference to this service. They have to do with delay in getting an appointment, delay in completion of work on the patient and delay in securing a report. These defects are, of course, primarily related to overcrowding. The general practitioner also complains that he often receives no report and later finds that the patient is returning regularly to the outpatient department, rather than back to his family doctor, for treatment. This not only leaves the general practitioner out of the picture but further adds to the load of the outpatient department.

There is evidence that in some instances the quality of work is beginning to suffer and the attitude of the doctor is changing. This statement is based on personal observation of limited and crowded space for examinations, inadequate histories and clinical observations and the testimony of administrators and others with opportunity of observing the work. For example, it is stated that, where formerly the consultants would stay as long as necessary to see all the patients who came in, they now stop when they have completed their three and one-half hour session. They now take the attitude that they are being paid on a time basis and the responsibility for the overload is not theirs.

Because of pressure in the departments, there is a greater tendency to make use of laboratory procedures as a substitute for adequate clinical observation. This further increases the burden on the x-ray and clinical laboratory and causes further delay. The material that comes into the department is excessive in amount and has been poorly screened by the general practitioner. Under these conditions it is not surprising that more patients are passed into the hospitals, resulting in overcrowding and long periods of waiting before definite treatment can be started.

Cottage Hospitals.—Cottage hospitals is a term applied to small hospitals in rural areas or smaller cities and towns. The term cannot be clearly defined since they vary from small institutions with a few beds to reasonably well equipped hospitals with 100 beds or more. In many instances they have been staffed by the general practitioners in the area, who have been able to follow their patients into the hospital and conduct their treatment. In some of the larger hospitals of this type, a certain amount of specialization has been developed. Many men have acquired a special skill, particularly in branches of surgery, and have become recognized as well qualified to do the work they undertake. While they have not completed a formal training program that is accepted as a requirement of specialization, they have been considered specialists and possess the equivalent skill and experience of the more formally recognized specialists. With the emphasis that is now being laid on specialism in medicine and the specialist classification under the Act, there is a tendency to displace these men with others from the general hospitals or teaching centers who have been recognized under the Act as specialists. In many instances these men have been assigned to the smaller hospitals on a part time or visiting basis, and in some instances they have been employed on a full time basis and have made their residence in or near the hospital. The purpose has been expressed by the Ministry of pursuing a policy of sending specialists out to the periphery. While no doubt the full use of specialists in the smaller hospitals is often needed and may result in improvement in the quality of the service, it is thought that the ultimate effect will be to further separate the general practitioner from the specialist and from the hospital. In order partly to meet the problem thus created, an intermediate group, termed Senior Hospital Surgeons or Senior Hospital Physyicians, has been created. These are employed on either a part time or full time basis but at a lower rate of pay than the full specialists. It is probably only a temporary expedient, and this group will gradually disappear. At present there is no well thought out policy. On the one hand, desire is expressed to elevate the position of general practitioners, but, on the other, the present emphasis on specialism tends to drive him out of the hospital altogether.

LOCAL HEALTH SERVICE UNDER THE ACT

Local Health Authority.—The second angle of the triangle of health coverage offered by the government is that administered by the Local Health Authority. The duties of this authority are defined in part III, sections 19-30 of the Act.[7] It is to be remembered that these services now offered were in the main already being rendered by the localities. Some that were permissive or were provided by volunteer agencies have been made mandatory but without additional means or facilities for making them more effectual. Prior to the Act there were 146 city and county health services administered by these localities. As previously noted, these services were financed from local rates plus a 50 per cent grant in aid from the central government. In certain areas economically below the average, an additional lump sum grant was made from the so-called equalization fund. In addition to their other activities, the local health authorities controlled and operated over 50 per cent of the hospitals and 85 per cent of the clinics. They are now directed to provide the following facilities and services:

1. Health centers.
2. Care of the expectant and nursing mothers and children of preschool age, including, in particular, dental care.
3. Midwifery service.
4. Health visiting services.
5. Home nursing service.
6. Vaccination and immunization service.
7. Ambulance service.
8. Prevention of illness and after-care.
9. Domestic help service.

The administrative body is the council of the county or city acting through a health committee of the council. In each area a Medical Officer of Health is employed as director of the services.

In some respects the activities and responsibilities of the local health authorities have been sharply curtailed. One thousand, five hundred and forty-five hospitals and 481 clinics previously operated by local health authorities have been transferred to the Regional Hospital Board. This transfer included all the tuberculosis sanatoriums and many of the convalescent homes and homes for the domiciliary care of the aged and the chronically ill. Tuberculosis officers and venereal disease officers, together with their clinics, were also transferred. The medical activities of the Department of Education still continue independent of the Act, at the local level, but are coordinated at the top, since the Chief Medical Officer to the Minister of Health and the Chief Medical Officer to the Department of Education are combined in one person. The effect of this transfer of facilities on the problem of tuberculosis is discussed later. The change brought about in the obstetric provision will be discussed in the section on General Medicine.

This disruption has made the Public Health Service less attractive as a career, and the number of students applying for courses in public health has dropped abruptly. The scope of activities of the Local Health Authority has been greatly reduced, and a medical career in this field has much less appeal. There is widespread discouragement among the personnel, founded partly on personal frustration but largely on the conviction that preventive medicine has suffered a serious setback. Many think that the Public Health Service is changing its objective and turning more in the direction of medical administration and industrial health.

Home Service.—The Act requires that a variety of home services be provided entirely without charge, including the attendance of a midwife, home nursing and a visiting health nurse. Domestic help may be provided, but here a degree of

caution enters and the Act states that with the approval of the Minister the local administration may collect a reasonable amount for this assistance, having regard to the means of those receiving this help. It is of interest that the hated "means test" should appear in this and other parts of an act written by the socialists. All persons performing the aforementioned duties are employed and paid by the Local Health Authorities. The Local Health Authority is also directed to provide prenatal and postnatal care for expectant mothers and to care for children up to school age with particular reference to priority dental attention. Dental care for school children is provided through the school health service under the administrative control of the Department of Education.

Certain comments are in order at this point. While these provisions exist on paper, they are to a considerable extent nonoperative because of lack of personnel, facilities and money. As noted elsewhere, the school dental service has broken down as a result of migration of the dentists into private practice. Many local volunteer organizations formerly aided in maintaining certain of these auxiliary services but have withdrawn from the field either because they have accepted in good faith the government's promise to provide this care or because they have taken the position that, since they are taxed to provide it, they are no longer under any moral obligation to make voluntary contributions for the relief of human suffering. One wonders how much confusion and conflict would result if such a system should become generally operative. Without any central directing agent the family will be advised on health matters by the midwife, the school health service, the visiting nurse and perhaps the family doctor. The expectant mother may attend a maternal welfare clinic, be attended by a midwife and then, in case of difficulty, be delivered by a physician who has no familiarity with what has gone before. Coordination of all these agencies supposedly will be brought about by conferences and committee meetings. It is evident that in the chaos of multiple agencies the influence of the family doctor will disappear. That this is an extravagant and wasteful system hardly needs stating.

Health Centers.—One of the main points emphasized in the socialists' medical program was the development of health centers.[9] The general scheme would provide one for each 20,000 persons. Under the Act it is the statutory duty of the local health authority to build, equip and maintain these centers. The Act further provides that facilities shall be available for any or all of a number of activities enumerated, including general medical service, dental and pharmaceutical service, specialist service, health education and all of the services that the Local Health Authorities are empowered or required to provide. The Local Health Authority is required to furnish all personnel except doctors and dentists, who will be paid by the Local Executive Committee. It is proposed that facilities for practice for the general practitioner will be furnished and that he will be charged a rental, not greater than the cost that he now sustains in operating his surgery.

Many details of the organization and structure of these centers have not been worked out 18 months after they were made a mandatory part of the plan. The conception, however, had considerable influence on the thinking of general practitioners and probably made many of them incline more favorably to the National Health Service Act as a whole.

The council of the British Medical Association reported at some length on this matter.[10] These reports favored the principle of the health center but advised that no general plan be adopted—they are to be developed gradually and for the present on an experimental basis.

Lack of funds and material have made it impossible to carry out any widespread program, even if there were any agreement within or without the Ministry as to the exact form the center should take. So far only three centers have reached the stage of construction. The center at Woodbury Downs is the only one that has advanced to the point that shows its ultimate outline. This is being constructed at a capital cost of about 150,000 pounds and will employ a staff of 64, including eight doctors together with dentists, pharmacists, nurses, midwives, home visitors and clerical personnel.

Any widespread extension of this type of facility is probably far in the future. When one translates the cost of building, equipping and operating 2,400 such centers into terms of a national budget, the project assumes astronomic proportions.

Ambulance Service.—One of the free services provided by the Local Health Authority under the Act is transportation of patients, either from within or without an area to hospitals or clinics. This may be either by ambulances or in "sitting cars." The transportation may be arranged by hospitals, municipalities or through voluntary organizations.

In London, under the London County Council, an unusually impressive and efficient ambulance service has been set up. This is operated from a central control station that receives calls and dispatches ambulances from the appropriate station nearest the point of need. This has proved to be of great value from the standpoint of efficiency in producing rapid and effective service and also has proved economical in operation.

In many areas we were informed of serious abuse of the service. Patients are being brought long distances in government transportation, either "sitting cars" or ambulances, for trivial and inconsequential reasons, and the demand on the service has increased tremendously. The law authorizes a paid attendant, if required. The purpose of this was to afford proper care of an ill patient while in transit, and this is also being abused. The provision of a service that is quite proper in spirit illustrates the difficulty of controlling abuse in a free service, where the recipient assumes no responsibility for the cost. Petty "chiseling" is widespread. Many persons are making considerable sums by furnishing patients with cars, and thousands of patients with attendants are being unnecessarily hauled around in all parts of England. In answer to a question as to how it was planned to control this evil, the answer was by simply cutting down the total appropriations for the service. This would deny the service not only to those who abused it but also to many who need it. To levy a small charge, which would be a much more effective control, is contrary to socialistic principles.

Tuberculosis.—The situation in reference to tuberculosis in England deserves special mention. While nationwide figures are not available, the general impression among doctors, and actual figures in certain areas, point to a definite rise in the tuberculosis rate. There are no doubt a number of causative factors, associated with the strain and stress of war crowding and nutritional limitations. Prior to the Act, the entire care of the tuberculous patient was under the Local Health Authority. This agency supervised the home care, both presanatorium and postsanatorium, and provided and supervised the hospital and sanatorium treatment. With transfer of hospitals and sanatoriums to the Regional Boards, responsibility has been divided. The tuberculosis medical officers, formerly employed by the Local Health Authority, are now jointly employed by the Authority and the Regional Hospital Board concerned and divide their time on an agreed fractional basis between these two employers. This is not a particularly satisfactory situation, although both parties are striving to coordinate their activities. Meanwhile, about 5,000 sanatoriums and hospital beds have become unavailable, because of lack of funds and personnel. There are now many tuberculous patients with positive sputum being treated at home, often under crowded conditions. Certainly it would appear that in the field of tuberculosis control, as in some other phases of preventive medicine, the Act has hampered rather than promoted the public welfare.

GENERAL MEDICAL SERVICE

Administration.—The general medical service is the third channel through which the Minister executes the Health Act. For the purpose of administration 138 districts have been created, each under the direction of an Executive Council directly responsible to the Minister. These councils or committees consist of a chairman appointed by the Minister and 24 other members, four of whom are also appointed by the Minister. Eight are appointed by the Local Health Authority, seven by the local medical committee, three by the local dental committee and two by the local pharmaceutical committee. The Minister is

9. National Health Service Act of 1946, part III, 21:(1).
10. Interim Report by the Council of the British Medical Association on Health Centers, July 1948. Report by the Council of the British Medical Association on Health Centers, 1949.

empowered to vary the constitutions of these councils whenever he sees fit. The special local committees representing the doctors, dentists and pharmacists can operate as such only after they have been recognized by the Minister.[11] There are six other particulars in which the Minister is empowered to issue regulations governing the constitutions and activities of these Councils.[12] It is the duty of the Executive Committee to organize and regulate the services performed by the general practitioner, the dentist, the pharmacist, the medical ophthalmologist, the ophthalmic optician and the dispensing optician. In pursuance of this they prepare lists of those legally qualified to practice in each of these branches and assign persons not on a list to some practitioner whose list is not complete. They make payments to dentists, pharmacists and those engaged in the supplementary eye service according to an agreed schedule. They distribute the total sum allotted to each area for the general practitioner on the basis of the number of persons on each list after making certain deductions. Through the Medical Practice Committee they regulate the admission of new doctors to an area. There are rather complicated provisions regarding the locating of new practitioners that involve the local Medical Practice Committee, the Executive Council and the Central Medical Practice Committee. A practitioner of medicine can locate in a certain area only with the consent of these boards. His request can be refused on the grounds that the area already has a sufficient number of practitioners. The Minister is empowered, if he is satisfied after making such an inquiry as he may think fit that adequate service is not being provided in any area, to dispense with any of the requirements or regulations under this part of the Act. Regulations are laid down governing action of the Executive Councils in cases of oversubscribing, failure to keep adequate records and lack of care in furnishing certificates. A special subcommittee of the Executive Council known as the Medical Service Committee deals with derelictions of a more serious nature, with particular reference to complaints of patients that provisions of the Act are not being carried out by doctors, dentists or pharmacists. Cases entered at this level may finally reach and be acted on by the Tribunal. The composition, duties and power of this body have previously been described.

The effect of these various regulations is to provide a means whereby pressure may be applied at will. It is true that little pressure has been applied so far, but the Minister can exert pressure whenever he so desires.

Distribution of Patients.—One of the principal criticisms aimed at the old system of medical service in Great Britain was the irregular distribution of physicians in reference to population. Applicable data were unavailable, but there is little doubt that distribution left much to be desired. To correct maldistribution, the new law has prohibited the sale of medical practices. Customarily in Great Britain physicians bought and sold practices usually in the range of one and one-half to two times the gross income received during the preceding year. Panels of patients under the old National Health Insurance Act tended to enhance these values. In the opinion of the planners such a system was inconsistent with a theoretically desirable redistribution of professional personnel, based on approximately equal numbers of population per physician. The National Health Service Act, therefore, abolished the sale of practices. However, a fund of 66,000,000 pounds was set up as remuneration to physicians for the goodwill value of their practices, a sum agreed on by the authorities and the British Medical Association as sufficient to liquidate this obligation on terms equal to one and one-half years' gross income. Here again, special regulations were formulated to govern eligibility, method of payment and interest rates. The significant fact was that ability to recover depended on agreement to participate in the National Health Service on or before the appointed day, July 5, 1948. Without question, this proviso and the conditions attendant on it were extremely powerful factors in forcing a reluctant profession to enter a system to which it had on several previous occasions expressed opposition.

The Act also created a Central Medical Practices Committee. This committee is appointed by and responsible to the Minister. It consists of nine members, seven of whom (including the chairman) are physicians, selected after consultation with the principal medical organizations. The construction of the Medical Practices Committee puts responsibility on the actively practicing medical profession for the staffing of the general medical services, and to that degree it is contended that governmental control is avoided.

Generally speaking, a physician may apply for and be permitted to settle in any location except where "the number of medical practitioners in the area or part of an area concerned is already adequate." If he applies and is refused, his only appeal is to the Minister. What then are the customary means open to a physician for entering a practice?

1. He may apply for a vacancy. Information is received from Executive Councils about understaffed areas or vacancies due to death, retirement or removal. These appointments are advertised in the medical and lay press. Local medical committees are consulted respecting the qualifications of candidates in terms of specific medical needs and conditions. Competition for vacancies is frequently heavy.

2. He may elect to serve as an assistant to an established practitioner, subject to regulation as regards size of lists and available patients.

3. He may receive financial inducement to settle in an isolated or otherwise undesirable area.

A special method of entry for recent graduates without hospital experience is to secure a 12 month appointment as trainee assistant to a qualified general practitioner. Such trainees receive grants of 700 pounds as salary and living expense, plus an additional sum of 150 pounds for car maintenance. The preceptor receives 150 pounds.

The machinery designed to improve distribution has not accomplished its purpose. In one city of a 1,000,000 population 49 per cent of the doctors care for 12.5 per cent of the population, 31 per cent of the doctors care for 56.5 per cent and 20 per cent of the doctors care for 31.0 per cent. These figures refer to a medical pool of 661 list holders and 74 assistants and further assume that most of these assistants work with the groups caring for the largest numbers of patients. Further substantiation is provided by data gathered by the British Medical Association, which has classified physicians by age groups and net remuneration from all sources. Of 5,251 doctors surveyed, approximately 29.5 per cent had net incomes of less than 1,000 pounds, the average for the group being 500 pounds, and 38.9 per cent net incomes in the 1,000 to 2,000 pound range, averaging 1,500 pounds. Above the 2,000 pound level, incomes may reach to 4,000 pounds or slightly more. Essentially the same story is repeated in an analysis of figures in a city of 120,000. These data demonstrate that the persistent problems in professional maldistribution are overlisting, which produces more income and less service, and underlisting, which gives the opportunity for good service at financial sacrifice. The significance of this relationship in terms of the quality of medicine received by the English people and the economic difficulties experienced by the majority of the profession is obvious. This has come about rather naturally. Probably 80 per cent of general practitioners in Great Britain had panels of varying sizes under the old National Health Insurance Act. Those in thickly populated industrial centers fell heir to their former panels, now considerably augmented by dependents. Doctors in residential or rural areas practicing private medicine for the most part attracted small lists and must now depend on private patients for supplementary income.

The prescribed maximum of 4,000 patients per list is exceeded in a number of areas as inevitable consequences of the changeover. The employment of assistants permits the addition of 2,400 patients for each aide so employed. It is doubtful whether assistants are exploited, since they are scarce and can command salaries commensurate with their value both in terms of the service they supply and the added income they produce.

To summarize, distribution is far from satisfactorily settled. The optimum ration of 3,000 patients per doctor as envisaged by the Ministry is still a theoretical objective. Actually the ratio of population per general practitioner is about 2,200. Since the global sums available for general medical services are fixed in relation to population, for every physician who earns more

11. Schedule Sixth National Health Service Act.
12. Schedule Fifth National Health Service Act.

by serving more than his equitable share of patients another must necessarily earn correspondingly less. The use of assistants to take care of expanded lists does not obscure the fact that a small percentage of physicians takes care of a substantial majority of the people. As income increases, so correspondingly must time and energy available per patient decrease. The small list holder has a better opportunity to serve his clientele, but to his own financial detriment.

This question is under negotiation. A reasonable solution would appear to be in the direction of increased capitation fees, with some differential in amount favoring the first thousand enrolled as against succeeding hundreds or thousands of enrollees. However, it is doubtful whether the country can afford any substantial additions to the present excessive costs of the program.

Methods of Payment and Income.—All persons desiring to do so may register on the list of a family doctor of their own choosing. As soon as the patient is accepted by the physician, a "medical card" is issued by the Executive Council. Former panel patients are permitted to transfer to the new list of the same physician without formal application. Once accepted, a patient cannot be dismissed from a list without his consent while under active treatment. The patient, on the other hand, can move about at will. Transfers are made by clerks who gain access in this way to medical data usually considered confidential. Since actual or threatened transfer not infrequently occurs because of a doctor's unwillingness to accede to capricious or unnecessary demands for service or supplies, this arrangement is criticized as not only wasteful but as having seriously lowered professional prestige and influence.

*Classification of Doctors According to Number in Practice and Levels of Net Annual Remuneration**

Net Annual Remuneration †	Unassisted		With 1 Assistant		With 2 or More Assistants		One of 2 Partners		One of 2 Partners with Assistants		One of 3 Partners		One of 3 Partners with Assistants		One of 4 Partners or More		One of 4 Partners or More with Assistants		Total in Each Income Group
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Under £700.....	2,288	28.9	32	2.8	..	..	1,128	22.5	32	5.6	430	19.9	11	5.9	206	18.5	5	4.1	4,132
£700- £1,000.....	1,181	14.9	39	3.4	..	..	756	15.1	25	4.4	329	15.2	20	10.7	160	14.4	3	2.5	2,513
£1,000- £1,300.....	1,154	14.6	76	6.6	..	..	793	15.8	49	8.5	364	16.9	14	7.5	185	16.6	14	11.6	2,649
£1,300- £1,600.....	1,136	14.3	98	8.5	4	26.7	716	14.3	56	9.7	300	13.9	23	12.3	194	17.5	12	9.9	2,539
£1,600- £2,000.....	1,127	14.2	200	17.4	1	6.7	734	14.7	110	19.2	329	15.2	35	18.7	155	14.0	23	19.0	2,714
£2,000 and over...	1,033	13.1	706	61.3	10	66.6	879	17.6	302	52.6	409	18.9	84	44.9	212	19.0	64	52.9	3,699
Total.....	7,919	....	1,151	....	15	....	5,006	....	574	....	2,161	.....	187	....	1,112	....	121	....	18,246

* Source: British Medical Association.
† The pound at the time this table was compiled was worth $2.80.

Payment for the general medical service comes from the Central Pool, which is created by allocation of 18 shillings from the Treasury for each anticipated user of the service; calculations are based on 95 per cent of the population. Mileage payments are made to rural practitioners to compensate them for travel and car expense in accordance with agreed on units which represent travel of a mile or fraction thereof for distances in excess of two miles.

The balance is allotted to the Executive Councils and forms "local pools." This money is available for distribution after certain first charges are made for:

1. Temporary residents, who are cared for at one-fourth the annual capitation rate out of a special reserve.

2. Emergency care, which is available to any patient by the nearest available doctor. Fees may be charged but are rarely submitted by reason of reciprocal arrangements between the physicians themselves.

3. Fixed annual payment. Newcomers into practice or any physician with a small list may apply for a fixed annual payment of 300 pounds. If approved, he accepts patients at six-sevenths the regular capitation rate. The intent is to supply an income of sorts until approximately 2,000 patients are listed, beyond which it becomes financially advantageous to revert to standard capitation fees.

4. Anesthesia administration.

The effect of these deductions is to reduce the rate per capita to the range of 14.2 to 16.2 shillings. Distribution occurs quarterly. Payments are calculated on the number of patients on a list as of the first day of the quarter.

There are, however, a number of ways by which a physician can augment his income.

1. From private patients. Actually, private patients are a negligible component in general practice and the numbers are steadily growing smaller. Repeated statements were received to the effect that "My private practice is next to nothing," or "I may have a dozen or so private patients left," or "The income from my private practice is less than 5 per cent of the total." A commonly added comment is that private patients are older persons who are accustomed to or need special attention and who can pay for it. A few younger individuals or families maintain private status, but the trend is decidedly away from it. The general practitioner as we met him was convinced that private practice will be a thing of the past in a few years and that the Act could have had no other logical outcome.

2. From inducement payments paid to a physician to encourage settlement in remote, sparsely populated or otherwise undesirable location.

3. From maternity services. For purposes of payment, maternity service is divided into two prenatal examinations, attendance at delivery and a postnatal examination at the sixth week. Physicians earn 5 guineas for these services to their own list patients. If a physician is registered with the Executive Council as especially qualified in obstetrics, the fee is raised to 7 guineas and applies to all patients, whether on his list or not. Although the Ministry proposes to encourage participatfon by general practitioners in the maternity services, several important factors militate against it. There are the services supplied through the Local Health Authorities—antenatal and postnatal clinics and the midwives' services. Midwives now take care of 80 per cent of normal deliveries, mostly in the home, and do it well. Curiously, the doctor's general supervision over the obstetric patient does not necessarily include the actual delivery—he may or may not attend, usually as requested by the midwife. Most abnormal obstetric cases are referred to hospitals for observation by specialists in obstetrics. In our opinion the general practitioner's function in obstetrics is of second rank importance.

4. From emergency drugs for which special allowances are made to pay for the cost of dispensing at times or in circumstances in which they are not otherwise available.

5. From other miscellaneous income, acquired through the training of assistants, industrial or clinic appointments, from special certificates, care of transients, vaccinations or similar services.

All sources considered, it is approximately correct to calculate an average general practitioner's gross income at 1 pound per patient on his list and his net about two thirds of that amount. If 2,200 patients represent the approximate ratio of population per physician in Great Britain, these figures would indicate that the average annual net income from a general practice at current rates of exchange would lie between $4,000 and $4,500.

Facilities.—The vastly expanded demand for medical services first converges on the surgery of the general practitioner. In theory his desk is the screen by which frank or suspected organic disease of serious proportions is separated from the larger accumulation of minor or ordinary complaints. For a variety of reasons, this important basic relationship is breaking down, with serious loss in the usefulness and prestige of the general practitioner.

Surgeries are customarily located in or near the practitioner's home, a fact of considerable importance to doctors' wives who act as unpaid receptionists, attendants and clerks.

There are one or more rooms for examinations and consultations, a waiting room and what remains of a dispensary for drugs and medical supplies. Installations of specialized laboratory equipment or apparatus are uncommon. The usual procedure is to devote one to two hours morning and evening to office practice. The balance of time is divided between home visits, care of private patients, industrial or clinic work and the like. Surgery hours must be conspicuously posted to conserve the time of all concerned.

The common complaint against this system by patient and physician alike is overcrowding. In a great many instances coming under our observation, numbers of patients seen in a two hour period were so great as to make effective medical service impossible. As a result of these large numbers, the tendency is to make excessive referrals to the hospital outpatient services. The same tendency appears to be growing in relation to the office performance of the rather commonplace forms of medical and surgical treatment.

General Observations.—The general practitioner now finds himself almost completely cut off from hospital connection. In the smaller towns and rural areas he may continue to administer anesthesia, to provide maternity service and to maintain some contact with inpatient care. The unmistakable trend is away from his direct participation in these activities. The separation of the general practitioner from modern hospital staff functions is recognized as one of the most serious defects in the existing health service. It is also agreed that deterioration in the general practitioner services is too great a price to pay for the correction of defects in hospital practice which could have been corrected along much simpler and more constructive lines.

Dispensing of drugs and medical supplies has largely disappeared from urban practice where prescriptions are filled at pharmacists' shops. In rural areas, outside the prescribed two mile limits, dispensing persists for which special fees are provided.

Much of the general practitioner's time and energy are given over to services which are essentially clerical in character. Certificates must be signed to permit registration under the health plan, to qualify for benefits under the insurance act, to support claims for change of employment and to provide extra rations, fuels, petrol and a great many other special authorizations which have some relation to a health situation. A great many are requests for admission to a hospital or outpatient department or for eye services, drugs, supplies or services provided by the Local Health Authority. The statement that a practitioner may see 30 to 40 patients at a session without using an instrument other than his fountain pen is not altogether fanciful.

The general practitioner in Great Britain as we observed him is no longer a free, independent professional person. He finds himself sharply circumscribed in function, in influence and in outlook. His work tends to become more superficial as he is increasingly concerned with clerical and technical trivialities. His importance in diagnosis, in treatment and in preventive medicine diminishes as these functions are increasingly taken over by specialists, health officials, midwives, hospital laboratories and technical services. His lack of association with the stimulating clinical atmosphere of hospitals and his inability to follow his own patient through the establishment of a diagnosis and course of therapy stultifies all the careful preparation he underwent in his undergraduate years for just these purposes. To what extent expansion of postgraduate teaching, the ultimate construction of health centers, restoration to certain hospital functions and improvement in his relation to patients and in his economic position will tend to correct his difficulties remains to be seen. There does appear to be a growing recognition that the professional potential of the general practitioner is not being used to best advantage. The correction of present defects will depend on a reappraisal of the function of the family doctor and his reestablishment as the backbone of medical service to the population at large.

Pediatric Service.—Pediatric practice in England is different than that of the United States. Prophylactic public health and general care of practically all children is done either by the Local Health Authorities or by the general practitioner. According to the National Health Act every child in the kingdom has his own doctor and is registered on the list of the general practitioner chosen by his parents. Theoretically the child is entitled to a medical examination at the doctor's office any time the parents so desire or to a home visit if the child is sick. Most mothers prefer one of the infant welfare stations operated by the Local Health Authorities.

The reason is that many mothers prefer waiting with other mothers and children at a welfare clinic rather than having a much longer wait in their own doctor's waiting room with sick persons. Not only must the mother wait her turn with the child for a period of one to two hours in an atmosphere not congenial and perhaps even injurious to the child's health but the very short consulting time that must be given each patient, even when the doctor is finally reached, makes this inferior to the care of the welfare clinic.

If the child is found to be sick at one of the welfare clinics, or by his own doctor, appropriate treatment is given within the physician's time and ability. If further pediatric advice is desired, the child is referred to the outpatient department of a hospital; if the child is ambulatory or if the child is sick at home, the physician has the right to ask for a home visit by a pediatric consultant. If hospitalization is necessary, it can be obtained only through the pediatric consultant.

In England, Wales and Scotland the pediatrician is the hospital full or part time consultant. He has arrived at consultant status by six to eight years' hospital pediatric specialization and is appointed to the hospital through the Regional Board. He practices usually part time at the hospital, working certain periods in the outpatient department and seeing patients referred by the general practitioners. He usually also has one of the pediatric services at his attending hospital and conducts various special clinics. In his remaining time he makes home calls in consultation with the general practitioners of his area and conducts his small private practice, if any. No child can be admitted to a hospital without going through the pediatric consultant either in the outpatient department or after a home consultation.

Pediatricians were relatively new as specialists before World War II and have increased in numbers and authority since the war. It must be emphasized that at the present time the bulk of pediatric care is in the hands of the local authorities and the general practitioner. However, many pediatric specialists will conduct some of the infant welfare clinics for the local authorities and do other pediatric work. Inasmuch as a community of 100,000 may have only one pediatric specialist, it can be easily seen that this field is far from thoroughly covered.

A word may be given here about private practice. There is almost no private practice in pediatrics among the general practitioners. Specialists will have a few children that are brought to them for paid treatment, but the factors that are driving out private practice from all medical care in Great Britain operate in pediatrics as well. These are the extra expense of drugs and medicines. As mentioned before, the private patient must pay the full cost of all medicines prescribed even though they are all citizens and have paid their share in taxes toward the National Health Act. The second drawback is the inability to obtain hospital beds for a paying patient and the extra cost. As one pediatrician stated, "I do not even bother to try to get any of my private patients into a hospital on a paying basis but just put them in the usual free ward beds and relinquish their care until the completion of their hospital stay."

The curve of mortality and morbidity has been steadily decreasing since the war, before the National Health Act, and it will be impossible to judge the effect of the Act according to the Ministry of Health for 10 years. However, certain generalities and trends can be noted. Unless there is a substantial drift of physicians from general practice and specialties to public health work, the prophylactic care of infants will probably not be bettered but will deteriorate. At the present time one rarely sees a malnourished child, and rickets and scurvy have disappeared. This is partly due to a campaign of many years for breast feeding (95 per cent of the newborn infants at 10 days of age are breast fed). There is, however, considerable tuberculosis among children. In almost every hos-

pital visited, cases of tuberculosis would number 10 to 15 per cent of the children's wards. This is almost entirely due to the shortage of beds for adults with active lesions who act as carriers. However, this is a holdover from the building destruction and shortage of nurses.

It is in the treatment of childhood defects that the National Health Act has caused the greatest changes. Instead of uniform direction resulting from close association with the Local Health Authorities over hospitals, proposals for any change must be agreed on by several hospital boards and in some cases with a number of teaching hospitals. The outpatient departments to which these ambulatory children must be referred are greatly overloaded.

The hospitals are filled to overflowing, and there are long waiting lists; fortunately, places can be found for acutely ill children in most hospitals. The waiting time for a tonsillectomy varies from 18 months to two years in all hospitals visited.

One of the most disturbing effects of the National Health Act is the breakdown or deterioration of the prophylactic dental treatment of the school child, owing to the serious loss of dental surgeons staffs who have transferred to the National Health Service. The introduction of the general dental service has indirectly caused irreparable damage to the teeth of hundreds of thousands of school children and may bring about, in the near future, the total collapse of all the priority dental services.

Many mothers would now rather bring children directly to a hospital clinic than have them under the care of their own doctor, to whom they should turn for advice. Some of this attitude is due to the confusion and overlapping of the services rendered by the four major agencies. For example, a newborn infant in the home will be under the care of a midwife, who is under the jurisdiction of the Local Health Authorities. Should the infant become sick, the mother is expected to call the general practitioner on whose list the infant has been placed. He is under the Local Executive Council through which he makes his reports and receives his renumeration. If the general practitioner feels that the infant is suffering from an illness about which he requires advice, he can call in a pediatric consultant who is under the jurisdiction of the Regional Hospital Board. If the child is ill enough to require hospitalization, the pediatric consultant may enter him in a regional hospital, or, if the consultant is on the staff of a teaching hospital, the child will be the responsibility of the Board of Governors of the teaching hospital. It is, therefore, possible in a case of simple gastroenteritis in a newborn infant to use the professional personnel of four different governmental agencies. This, obviously, does not help toward the personal feeling and sense of responsibility that a doctor is accustomed to feel toward his patients.

If the American mother can visualize her baby's being delivered in a maternity or general hospital with ward care or at home by a midwife (a graduate, qualified obstetric nurse) and then taking her baby to an infant welfare station for its infant years and to a preschool station or nursery school for his childhood period, she has an idea of national care. Medical examinations will be done in school clinics and immunizations by public health doctors and nurses during his or her school life; if any acute illness should occur, medical attention will be received similar to that given by the city or county health department physicians in our country today.

Pharmaceutical Service.—Each Executive Council is required to prepare a list of those who are entitled to dispense medicines or to supply materials and appliances available under the Act. All drugs and appliances are furnished without cost except to the private patient. Any pharmacist has the right to apply to have his name or firm included in the list of those supplying medicines at government cost and to withdraw from the list three months after he has given notice of his desire to do so. Prices are fixed by a price bureau, one being set up in each of 13 regions. The joint pricing committee for England coordinates the work of the 13 price bureaus. The pharmacists locally are represented by a local pharmaceutical committee, which deals with the Local Executive Committee in controversial matters.

This service has proved to be very costly. The budget for 1949-1950 is 19 million pounds, but this will be considerably exceeded. One hundred and eighty-seven million prescriptions were dispensed in England and Wales the first year, or an average of four and a half for each member of the population. The average in Scotland is lower, being about three and a half per person. The proposal to charge a shilling for each prescription has not gone into effect, partly because of difficulty in administration and partly because it was very unpopular. These prescriptions include not only drugs but appliances and various articles for the use of the sick. Over the counter buying of simple remedies has practically disappeared, since they can be obtained free on prescription. The incessant demand for medicine has added greatly to the heavy burden of the practitioners. This does not represent the total drug bill, since many rural physicians still dispense their own drugs. The pharmacists state that they are not profiting by their increased business but are working harder for about the same income.

Supplementary Eye Service.—The ultimate objective under the law is to develop ophthalmic service in hospitals and clinics on a sufficient scale to care for the needs of the population in this particular field. The available facilities for accomplishing this are limited. To overcome this difficulty a supplementary eye service has been established under the Local Executive Councils. The regular service is being developed under the Regional Hospital Boards. This division of direction has been rather confusing. It is planned that the supplementary service will ultimately go out of existence. Each Executive Council has created an Ophthalmic Service Committee, which is charged with the duty of organizing the service and of making up the lists of ophthalmologists and practicing opticians qualified to render service under the Act. Everyone is entitled to this service, including examinations of the eyes and the supply of glasses, either through the specialist clinics or the supplementary services. The rate of payment to the specialists and the practicing optician was set by a special committee as in the other services.

The demand for this service has been overwhelming and there is a large backlog of unprovided examinations and unsupplied glasses. At present the lag is about six months, although the Ministry estimates that this backlog will rapidly decrease. As of October 1949, three million pair of spectacles were on order and 5,250,000 had been supplied. In February 1950 the demand had not receded and the waiting period was still about six months.

Most of the examinations are made by practicing opticians, since they out-number the doctors rendering this service six to one, (5,662 to 963). The supplementary ophthalmic service is estimated to cost over 12 million pounds, but this figure will probably be greatly exceeded. This also does not include the specialist service in hospitals and clinics.

Criticisms of this service were common, based on both the excessive demands and the hurried and inadequate nature of the examinations performed. To what extent the eye program has met a real need and to what degree it represents waste is imponderable. Certainly there are many more urgent medical needs for which adequate provisions are not being made.

Dental Service.—Under the Act, dental care is provided without cost to the patient. It is paid for on a fee-for-service basis by each local executive committee. The scale of fees was established by a committee [13] and was based on the assumption that a dentist could be expected to work 33 chair hours per week and that appointments would average 30 minutes each.

The demand for dental service soared enormously after July 5, 1948, and dental incomes increased to such a degree that the Minister ordered a 50 per cent reduction in fees on earnings in excess of 4,800 pounds. This answer of the Ministry penalized both the good and the bad. It is clear that a larger income could be gained by a dentist doing good work but working longer hours or shortening the time of each appointment, taking more patients and doing inferior work. A particularly skilled and rapid worker might increase his income by both lengthening his hours of work and shortening his appointment time and still do good work. The urge to work longer hours and to develop special skill in order to gain additional income would seem commendable if the quality of work is good. Through such effort the backlog of dental need could be more

13. Report of the Inter-Departmental Committee on the Remuneration of General Dental Practitioners, London, His Majesty's Stationery Office, 1948.

quickly met. But that is not the way socialism works. Without differentiation between the honest and the venal, a straight cut was made applicable to all.

If a practicing dentist finds that any but the simplest procedure is required, he has to submit a statement and proposal to the Dental Estimate Board. After due consideration this permission may be granted or may be refused. The dentist may be directed, for example, to extract teeth rather than make a partial replacement. The machinery of the Dental Estimate Board grinds rather slowly, and needed work is delayed.

One unfortunate effect of the present system of dental care has been the collapse of the preventive dental care in the school system. The dentists employed to carry on this work have been attracted by the greater rewards of private practice and have left the school service in large numbers. Their salaries cannot be materially raised without dislocating the entire salary scale in the Department of Education. Thus one sees a peculiar but rather typical flowering of a system which, in planning everything for all, provides unlimited corrective and restorative privileges but seriously cripples work in the preventive field.

The cost of the dental service has far exceeded expectations, and at present there is no indication that the demand is falling off. The estimate for 1949-1950 was over 28 million pounds. The exact figure is not known but will be much greater.

GENERAL CONSIDERATIONS

Question of Cost.—The estimate of cost of the service in Great Britain for the year 1949 to March 30, 1950, was 352,324,600 pounds. It is thought that this will be exceeded by a considerable but yet unknown amount.[14] This does not include heavy maintenance, replacements or capital expenditure for expansion. It does not include any material amount for the promised health centers, an item of about 350 million pounds. Estimates for 1950-1951 will be higher, judging from the opinion of numerous persons connected with hospital management and Regional Boards throughout the country. The total cost has far outstripped all estimates, and there is no evidence that the peak has been passed. It is interesting to note that in the Beveridge Report it was estimated that a comprehensive health service would cost 170 million pounds. The cost of dental and ophthalmic services is equal to that of the general practice service, and both of these are operating without any brake on their activities. The demand for hospital beds is unsatisfied. All general hospitals have long waiting lists, in some categories as long as two years. Scarcely a start has been made on the program of health centers. Outpatient departments are bulging. The surgeries of the general practitioner in the industrial areas are overcrowded, and their facilities are grossly inadequate. The need for capital expenditure is everywhere pressing. The funds available for medical care have been dissipated on services that, while to some extent are desirable, are not essential, and essential services have suffered.

The health of the people is conditioned by many things other than medical care, such as housing, nutrition, clothing, health education and certain environmental factors. No people's economy can provide the maximum amount in each field, so that there must be a wise division of a nation's resources and an intelligent use of the amount available in each particular category. In spite of the great amount expended for medical care in England, there is no present evidence that it has in any significant way improved the health of the people or added to their happiness. Perhaps it is too soon to reap the dividends, for we were told not to expect them for 10 or even 20 years, a long time to wait for the outcome of an expensive experiment.

Central Purchasing.—Concern has been expressed in many quarters over the possibility of the establishment of a central purchasing agency. It is felt that, while this might be desirable from the standpoint of economy in the field of ordinary supplies, if it is carried into the purchase of technical equipment it might be extremely objectionable. The natural corollary to the mass purchasing of technical equipment would be to establish fixed standards and to let contracts to a single or a limited number of manufacturers. This would eventually tend to discourage improvements in technical equipment and to freeze technical advance. There is already evidence that this policy is being pursued. Two hearing aids have been accepted by the Ministry and are being dispensed through the usual channels. There has been considerable insistence that a purchasing officer be employed in each hospital. Statements were received from many sources that central purchasing is to become an established policy. When the state has a practical monopoly on the means of producing medical care, the possibilities of abuse are enormous, particularly if the monopoly extends to the production and distribution of drugs, equipment and other medical supplies.

14. Since this was written a deficit of 98 million pounds has been disclosed.

COMMENT

Any discussion of the National Health Service must be with the understanding that it is an integral part of the over-all National Social Security system of England. Policy is dictated by the necessity of fixing this keystone in the arch of the total social security plan rather than any hope of greatly improving the health of the English people now or in the foreseeable future. Prior to the passage of the Act, the local authorities furnished most of the medical social services now available. There are now no more medical facilities or professional personnel than before. In fact, 50,000 hospital beds, including 5,000 for tuberculous patients are now nonoperational. There is much evidence that the facilities were operating before the "day" more efficiently and at less cost than they are now. Much of the professional care was then furnished without cost, and millions of persons had demonstrated their willingness and ability to pay part of the cost by joining contributory schemes.

The British Medical Association had urged the extension of national insurance to the dependents of workers, the establishment of health centers on a gradual and experimental basis and the unification of the hospital system on a regional basis. Their objectives could have been accomplished without upsetting the house of medicine.

The Beveridge report [3] laid down the fundamental basis of an over-all plan of social security in three assumptions. It stated, "No satisfactory scheme of social security can be devised except on the following assumptions:

1. Allowances for children up to the age of 15 or if in full time education up to the age of 16.
2. Comprehensive health and rehabilitation service, for prevention and cure of disease and restoration of capacity to work, available to all members of a community.
3. Maintenance of employment, that is to say avoidance of mass unemployment."

In discussing the medical aspect later it states, "The primary interest of the Minister of Social Security is not the details of National Health Service or its financial arrangements. It is to find a health service which will diminish disease by prevention and cure and will insure the careful certification need to control payments, at the rate proposed in this report." [3]

One is justified in believing that the primary and compelling motive behind the present National Medical Service Act is not to establish a better system of medical care but a better controlled one; one that can be made to aid more effectively in carrying out the over-all social security plan. It follows then that arguments based on medical grounds such as comparative cost, waste, medical inefficiency, quality of care, standards of practice, effect on medical ideals and the destruction of private practice and of private initiative may be ineffectual and we must come to grips with the fundamental concept of the socialist state. There are, however, many idealists who do believe that the medical welfare of the people as a whole can be advanced through complete state control, and it is to these that reasonable arguments must be presented.

The system that prevails in England today is certainly not all bad, but most of its virtues are those of the medical social services that existed before the Act.

1. It has accomplished the unification of a disordered hospital system and established a regional control oriented around teaching centers.
2. It has removed the financial barrier, but this at present has benefited the middle rather than the low income group.
3. It has established a better income level for many hospitals, but it has not provided any means of expansion of facilities.

This increased income has been accompanied with increased operating cost and the imposition of a burden of work that is difficult to manage with present facilities.

4. It has made the services of consultants more readily available outside the hospitals and clinics. This has been of practical benefit in areas distant from the large hospitals.

5. It has further widened the gap between the specialist and the general practitioner and further degraded the position of the general practitioner.

6. It has to a large extent destroyed private practice.

7. It has produced a greater inequality of distribution of doctors in proportion to population, and it has further rendered success in the practice of medicine depending more on quantity than quality and has diluted the quality of medicine.

8. It has added nothing so far to preventive medicine but has disrupted public health work and produced serious problems in tuberculosis control and preventive dentistry.

9. It has added greatly to the cost of medical care, and it has thrown a great additional load on the medical facilities of the country at a time when these facilities were already burdened and hampered, after 10 years of war and postwar effort.

10. It has failed in its primary objective of effective certification control under the comprehensive insurance plan.

11. It has created an almost complete autocratic control of medicine through concentration of financial power in the central government and the authority given the Minister to govern by directions having the weight of law.

The development of a unified and coordinated hospital system is a desirable objective. This has, to a considerable extent, been accomplished on paper but is far from being a reality in the field of practice. As we understand it, a coordinated system of hospitals would mean hospitals of different sizes adapted to the requirements of the several communities and so distributed as to meet the needs of all the people. They should be so organized as to filter out at the lower level minor or self-limiting cases but to allow the flow of the more seriously ill and the problem cases into the large general hospitals prepared to carry out complete investigation and treatment. At present, there is no proper screening and the general hospitals, with their high operating costs, are engaged in caring for thousands of patients that should be treated at the level of the general practitioner or the cottage hospital. There appear to be no funds available for improving or extending hospital facilities.

The financial barrier, as far as the individual is concerned, has fallen. The patient has access to medicine as it is, but he is paying for it in extra taxes, leaving less for food, clothing, shelter and recreation. The low income group had access to as good, or better, medical care before the Act—either through insurance or the free service of the clinics and hospitals. The middle income group who were accustomed to paying their way are benefited financially.

The voluntary hospitals were in serious financial difficulty before the Act for reasons previously mentioned. Their level of income has increased, and they have been relieved of the burden of deficits that harassed many of them. Some of them also were relieved of adequate endowments. At the same time operative costs and administrative costs have increased a great deal, more in these hospitals than in privately operated hospitals. The large group of voluntary helpers has been lost, and the flow of money from voluntary contributory schemes has dried up. The actual cost to the British people of producing a day of hospital service has increased sharply. Despite this, there is no evidence that the quality of service has improved, and on the basis of present facilities the quantity cannot. Furthermore, because of the lack of a proper screening process, the massive and expensive efforts of the great general hospitals are to a considerable extent being wasted on trivialities. They are killing mosquitoes with 10 inch guns.

The greater availability of consultants has been beneficial, although the problem of how to use the consultants in the smaller hospitals has not been worked out. As the plan is developing it may do great harm to medicine and medical care by destroying that very considerable group of able men that stand between the general practitioner and the fully qualified and accredited specialist.

The tendency of the present system is to degrade the general practitioner to the level of a clerk, a signer of certificates or a guidepost to the specialist. If the specialist moves out to the periphery and takes over the activities of the smaller hospitals, the general practitioner will have little opportunity or incentive to improve his status and to progress as a physician and a scientist. The middle group, the ladder between the general practitioner and the specialist, will be ground out, and two types of doctors will develop—quite different in their understanding, their needs and their objectives. Medicine will become hopelessly divided.

There may be differences of opinion as to the advisability of destroying private practice, but there is little question that the effect of the Act, whether by chance or design, is to destroy it. The limitation on private rooms in government hospitals and the inordinate rise in cost make it increasingly difficult for the private patient to survive. The small number of private patients and the restriction placed on physicians' fees in government hospitals make existence for the private practitioner precarious. Private practice, unhampered by discriminatory rules, if allowed to exist alongside public medicine, could survive, but its very existence would be a constant reproach to the architects of public medicine.

Distribution of doctors in relation to population in a free society is governed by many factors, such as access to facilities, economic advantages, social compatibility and general attractions presented by various communities. Under the present English system, the maldistribution that existed before the Act has been definitely aggravated as has been shown in the body of this report. The reasons for this are easily understandable and should have been easily foreseen. Its correction without complete state control of location and elimination of free choice of a physician will be difficult to accomplish. An equal division of the people among all the general practitioners would give each doctor a net income from practice of about 1,500 pounds, or at the present rate of exchange about $4,200. Such a distribution does not exist, however, and more doctors are below this average than above it. Many of those below are among the best qualified and are suffering real hardship. The majority of the people are being cared for by doctors with large lists, and it is impossible for these doctors to give adequate service. The fact is attested by observation of crowded offices, conveyer service, the inordinate number of referrals to outpatient departments and overloaded hospitals. The center of gravity of medicine has shifted, and the emphasis is on numbers rather than service. A physician can no longer gain recognition by rendering better service and thus secure a financial reward in a paying private practice. If he is to survive financially, he must gain in numbers at the sacrifice of quality of service. Many fine and thoughtful physicians are caught in this dilemma and are striving to maintain standards and numbers by means of hard work or are suffering a frustration of spirit almost intolerable. Others have adjusted their conscience to their economic needs. Others are unaware that there is any problem. As time passes and a new generation untaught in the traditions of medicine arise, there will surely be less agony of spirit among the doctors and more agony of flesh among the patients.

The effect on the Public Health Service operating through Local Health Authorities has been most unfortunate. The service has been disrupted, and its personnel is discouraged and disgruntled. The hospital service, previously controlled locally, has come under control of the Minister and through him of a new and separate body—the Regional Hospital Board. The previously well integrated tuberculosis service has been divided, and the tuberculous patient in course of treatment may come under three separate agencies of the government. The same thing has happened to the maternity welfare program. A pregnant woman may be under three separate agencies of the government and her newborn child under a fourth. Having hamstrung a going concern in the field of public health, the new service has so far contributed nothing in the realm of preventive medicine.

The additional financial burden placed on the people of Great Britain is difficult to estimate, as only a portion of the bill has been rendered. The still undisclosed deficit for the year 1949-1950 will eventually come out of the pockets of

the people who are now so carelessly wasting their medical resources. The elimination of the barrier of common sense along with the economic barrier has imposed an impossible load on the creaking machinery of medicine. A 10 year deficit in normal expansion plus 10 years of aging left England in 1948 with medical facilities barely able to carry a normal load. On this machine was imposed a greatly increased demand—a demand that it is not capable of meeting. To pretend that the overcrowded office, the congested clinics and hospitals and the long waiting lists are evidences of a successful system of medicine is absurd. The waste of money on the uncontrolled use of drugs, appliances, ambulance service and other accessories of medicine while 5,000 beds for tuberculous patients are closed would seem ridiculous if it were not pitiful.

The Beveridge Report[4] particularly stresses the necessity of "careful certification needed to control payment" under the insurance act. Evidence is convincing that in this respect the National Health Service Act has failed. Absenteeism is increasing, rather than diminishing. This has occurred during a period when there has been a succession of two unusually mild winters and remarkable freedom from epidemic disease. The answer is found partly in the fact that the insurance allowance for sickness may equal the wages in certain low income groups, but more particularly in the changed relationship of the patient and doctor. The patient is in a position to demand what he wants. He has an economic weapon that he does not hesitate to use. If he is not granted what he demands, whether it is an ambulance ride, a drug, reference to a hospital or a certificate, he can remove himself, his family and his friends from a doctor's list. The doctor has completely lost his independence, since he can no longer gain economic freedom outside the medical monopoly established and controlled by the state.

Powers of the Minister—The most amazing and disturbing provision of the Act, however, is the one that defines the default power of the minister. Subparagraph (1) of part VI, section 57, reads as follows:

"Where the Minister is of opinion, on complaint or otherwise, that any Regional Hospital Board, Board of Governors of a teaching hospital, Hospital Management Committee, Executive Council, Ophthalmic Service Committee or Local Health Authority, or the Medical Practice Committee or the Dental Estimates Board have failed to carry out any functions conferred or imposed on them by or under this Act, or have in carrying out these functions failed to comply with any regulations or directions relating thereto, he (the Minister) may after such inquiry as he may think fit, make an order declaring them to be in default."[7]

If any agency whatever operating under the Act is declared in default, the Minister is empowered to make such orders as he may deem necessary against the party in default, and, in event of failure to comply with any directive in such manner and within such time as he may direct, he may take over their functions temporarily or permanently. It further allows him to charge any cost of this procedure to the party in default and, if necessary, seize his entire physical assets. Under this provision the Minister has adequate power to seize and himself operate any teaching hospital in the country if any action of its Board of Governors runs counter to the opinion or desires of the Minister.

Action on his part does not have to be founded on proof of dereliction but merely on the opinion of the Minister. When to this power is added his complete control of finances, it is evident that the whole machinery of decentralization is a sham and that not a shred of real authority resides anywhere except in the Minister.

The Act is replete with statements that explicitly refer to the final authority of the Minister. "The Minister may, after consultation with the Central Health Service Council, by order vary the constitution of the Council." The Regional Hospital Boards are appointed to administer the hospital and specialists service in their areas. They are directed to submit a scheme of operation. If, however, they submit a scheme that does not meet the full approval of the Minister, "the Minister may himself prepare a scheme and it shall have effect as if it had been submitted."

The same authority is granted the Minister by the Act to impose a scheme of his own on any Local Health Authority. Debate over details of a plan and especially as to the constitution of committees and boards seems futile in view of the completely overshadowing power of the Minister.

THE FUTURE OF MEDICINE

One cannot help taking a pessimistic view of the future of medicine in England unless the government radically changes its basic attitude toward medicine. The concept of comprehensive medical care without some direct payment by the consumer is fundamentally unsound. It makes little difference whether it is financed by direct taxation or by payroll deductions. If completely free to the patient it eventually results in such serious abuses that its primary purpose of providing good medical care for everyone is vitiated. Sooner or later the system will corrupt both the receiver and dispenser. When it is wedded to an over-all security payment as in England, its evil possibilities are compounded.

Most of the doctors and many administrators are conscious of the defects of the system pointed out in this report. One repeatedly hears glib or at times apologetic reference to "labor pains," "teething trouble" and "growing pains" as an explanation of the present failures of the service. The dreamers, on the other hand, visualize a time when human nature has changed so radically that the patient will not abuse the service and doctors will all be imbued with such a spirit of good will that no other incentive to excel will be needed. No doubt, this ideal will be realized in the millennium. Meanwhile something quite different is happening.

Abuses of the service are evident everywhere, and they must lead to more and more regulations, tighter enforcement, greater penalties for violation, further limitations on freedom and further deterioration of the quality of medicine. In the end the great consumer group will suffer most. Sad as is the state of the practitioner of medicine in Britain, the plight of medicine itself is more serious; but what is most to be deplored is the present and future effect on the quality of medical care received by the English people. "Where there is no vision the people perish."

Appendix

Acts Under Which Certification is Required

Agricultural Wages Act
Births and Deaths Registration Acts
Catering Wages Act
Control of Employment Order
Control of Leather Goods Order
Control of Rubber Tyres Order
Disabled Persons Act
Food Rationing Order
Lunacy Act
Milk Order
Personal Injuries Act
Coal Haulage Wages Act
Services and Mercantile Marine Disability Pensions Acts
Wages Councils Act
Welfare Foods Order

Official Notes

ASSOCIATE SECRETARY OF COUNCIL ON MEDICAL EDUCATION AND HOSPITALS APPOINTED

Dr. Francis R. Manlove of Philadelphia has been appointed Associate Secretary of the Council on Medical Education and Hospitals. Dr. Manlove is a graduate of the Temple University School of Medicine. After interning at the Temple University Hospital, he served a fellowship in internal medicine at the Mayo Foundation, Rochester, Minn. For the past four years he has been assistant professor of medicine at the Temple University School of Medicine and during the past year, Chief, Medical Service B, Episcopal Hospital, Philadelphia. Dr. Manlove is a specialist certified by the American Board of Internal Medicine.

GOVERNMENT SERVICES

Navy

Training Duty for Naval Reserve Ensign (HP) Officers

A limited number of billets are open in naval hospitals to undergraduate medical students holding the rank of ensign (HP), U. S. Naval Reserve, who desire to volunteer for 14 days' active training duty with pay during the months of July, August and September (1950). Eligible are members and nonmembers of volunteer Naval Reserve units who will be assigned to a hospital nearest their home. Provisions have been made for the training of these officers on the various professional services. Members of volunteer units and nonmembers should submit applications to the commandant of their home naval district. Quotas have been assigned to all naval districts within the Continental United States, including the Potomac River Naval Command.

Duty Under Instruction

The following medical officers have been nominated for duty under instruction in the Navy's Graduate Training Program:

Comdr. Virgil A. Beuerman, to a residency in ophthalmology, Illinois Eye and Ear Infirmary, Chicago.
Comdr. George M. Davis Jr., to a residency in internal medicine, Naval Hospital, San Diego, Calif.
Lieut. Comdr. Stanley J. Okulicz, to a fellowship in urology, James Buchanan Brady Foundation, New York Hospital, New York.
Lieut. Charles F. Climie Jr., to a residency in obstetrics and gynecology, Naval Hospital, Portsmouth, Va.
Lieut. (jg) Willard P. Arentzen, to a residency in pathology, Naval Medical School, Bethesda, Md.
Comdr. Paul Deranian, to a residency in general surgery, Naval Hospital, Great Lakes, Ill.
Lieut. Comdr. William W. Manson, to a residency in obstetrics and gynecology, Naval Hospital, San Diego, Calif.
Lieut. Dale B. Watkins, to instruction in internal medicine, University of Pennsylvania Graduate School of Medicine, Philadelphia.
Lieut. (jg) Thomas H. Taber Jr., to a residency in orthopedic surgery, Naval Hospital, St. Albans, L. I., New York.

Award to Captain C. C. Shaw

Captain C. C. Shaw (MC, USN), director, Research Division, Bureau of Medicine and Surgery, was recently presented with the Certificate of Merit and the Selective Service Medal by Major Gen. Lewis B. Hershey, Director of Selective Service, in appreciation of his services as consulting internist to the State of Vermont Draft Board from 1940 to 1941.

Medical Missionary

A Presbyterian medical missionary, who requested immediate active duty with the U. S. armed forces in Korea after being forced to leave his missionary work in Taegu, Korea, has been given dispatch orders to active duty by the Bureau of Naval Personnel. He is Dr. Howard F. Moffett, of Savanna, Ill., who holds a lieutenant's commission in the Naval Medical Corps Reserve as a result of service during World War II. Dr. Moffett returned to Korea as a medical missionary last year, after serving on active duty as a naval reserve officer from April 1943 to March 1947. After being evacuated to Tokyo with other U. S. nationals, Dr. Moffett requested that he be ordered to active duty as a Navy medical officer attached to the U. S. Air Force. He was born on Aug. 16, 1917, in Pyengyang, Korea, where his parents were serving as Presbyterian missionaries.

Personal

Lieut. (jg) James F. Pierce (MC, USNR) of Westville, Ill., Comdr. Howard K. Schwartzfeld (MC, USNR) of Newark, N. J., and Lieut. James W. Birss (MC, USNR), of San Diego, Calif., have been recalled to active duty at their own request.

Veterans Administration

Tuberculosis in Veterans

Case records of World War II veterans whose applications for compensation for service-connected pulmonary tuberculosis have been rejected will be reviewed automatically to determine whether they qualify for benefits under the recently enacted Public Law 573, Veterans Administration has announced.

The new law increases the "presumptive period" for tuberculosis from one year to three years from date of discharge from the armed forces. Presumption of service connection means that, in the absence of evidence to the contrary, a disease which becomes manifest within the specified period to the extent that it is at least 10 per cent disabling is presumed to have had its origin while the veteran was in service.

The new law also applies to Spanish-American War veterans, and their rejected claims also will be reviewed. World War I veterans are not affected, since they were granted a comparable presumptive period some years ago. In the case of claims filed prior to June 23, 1950, effective date of the new law, payments on awards will be retroactive to that date. Awards on claims filed later will be effective from date of claim

Miscellaneous

U. S. Physicians to Visit British Atomic Research Center

Twelve medical and radiology authorities representing the United States atomic energy project will visit the British Atomic Energy Establishment at Harwell, England, early in August. All of the twelve were in Europe to attend either the Fifth International Cancer Congress in Paris, France, July 17-22, or the Sixth International Congress of Radiology in London, England, July 23-30, 1950. While at Harwell, the American group will be conducted through the laboratory and will hold discussions with laboratory personnel on matters of common interest in the field of health and safety.

The visitors are:

Dr. Shields Warren, Director, Division of Biology and Medicine, AEC, Washington, D. C.
Dr. Robley D. Evans, Professor of Physics, Massachusetts Institute of Technology, Boston.
Dr. Gioachinni Failla, Department of Radiology, Columbia University, New York.
Dr. Jacob Furth, Chief, Patbology Section, Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tenn.
Dr. Joseph G. Hamilton, Co-Director, Medical, Physics & Biology Divisions, Radiation Laboratory, Berkeley, Calif.
Dr. Alexander Hollaender, Director, Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tenn.
Mr. Leonidas D. Marinelli, Radiological Physics, Argonne National Laboratory, Chicago.
Dr. Leslie F. Nims, Chairman, Biology Department, Brookhaven National Laboratory, Upton, N. Y.
Dr. Robert S. Stone, Medical School, University of California, San Francisco.
Mr. Lauriston S. Taylor, Chief, X-Ray Section, National Bureau of Standards, Washington, D. C.
Dr. Paul C. Aebersold, Chief, Isotopes Division, AEC, Oak Ridge Operations Office, Oak Ridge, Tenn.
Mr. Logan Emlet, Superintendent, Operations Division, Oak Ridge National Laboratory, Oak Ridge, Tenn.

During the forthcoming visit to Harwell, Drs. Warren, Failla, Taylor, Hamilton and Evans will continue with British and Canadian representatives some of the discussions held last September 29-30, when 11 medical and radiology experts representing the United States atomic energy project attended a three nation conference on standards of radiation tolerance at the Canadian Atomic Energy Establishment, Chalk River, Ontario, Canada.

MEDICAL NEWS

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CALIFORNIA

Institute Grants for Cancer Research.—Grants-in-aid for cancer research totaling $52,433 have been made by the California Institute for Cancer Research to the School of Medicine at the University of California at Los Angeles. The institute's contribution covers the fiscal year ended June 30 and was used to finance several projects in cancer research at the university. The California Institute for Cancer Research, a nonprofit corporation aimed at providing funds for research into the causes, detection, diagnosis and cure of the disease, was formed in 1945. Since its inception the institute's efforts have brought to the school of medicine nearly $900,000 for cancer research. Currently housed in temporary quarters it has provided on the university campus, the institute will be located in the cancer research wing of the new medical school on its completion. Funds raised by the institute will be used to equip this unit and to provide financing for the maintenance of research projects on a long range basis.

COLORADO

Three Physicians Promoted to Department Heads.—Three promotions on the faculty of the University of Colorado School of Medicine have been announced. Dr. Ewald W. Busse has been appointed director of the Division of Psychosomatic Medicine; Dr. Charley J. Smyth will assume directorship of graduate and postgraduate medical education and Dr. Henry Swan II will be head of the department of surgery. Dr. Busse received his M.D. from Washington University School of Medicine in St. Louis in 1942. After an internship at St. Louis City Hospital, he entered the army in 1943, working in the field of neuropsychiatry. In 1946 he joined the faculty at University of Colorado School of Medicine. In addition to being director of the Division of Psychosomatic Medicine, Dr. Busse is chief of the Electroencephalograph Laboratory at the Medical Center, special consultant in neuropsychiatry to Denver University and Veterans Administration consultant in electroencephalography and psychiatry.

Dr. Smyth is a graduate of Jefferson Medical College, Philadelphia (1935). He was assistant physician for the Rackham Arthritis Research Unit at the University of Michigan and subsequently medical director at Wayne County General Hospital in Detroit. Dr. Smyth came to the University of Colorado in 1949 as assistant director of graduate and postgraduate medical education and assistant professor of medicine. During his professional career he has done extensive research in arthritis and rheumatism.

Dr. Swan studied at Harvard Medical School, Boston, where he received the M.D. cum laude in 1939. He took his internship and residency at Peter Bent Brigham Hospital and Children's Hospital. During the war he was chief of the surgical team, 5th Auxiliary Surgical Group. Dr. Swan has been at the University of Colorado since 1946; he is now professor of surgery. In addition to his new position, he is director of the Halsted Laboratory of Experimental Surgery and of the Cardiovascular Pulmonary Research Laboratory. He is consultant in surgery at Fitzsimons General Hospital and Fort Logan and Grand Junction veterans hospitals.

DISTRICT OF COLUMBIA

Eye Bank Affiliates with Hospital.—The George Washington University Hospital has become affiliated with the Eye-Bank for Sight Restoration, Inc., New York, which collects, preserves and distributes healthy corneas from human eyes for transplanting to blind persons who have lost their sight because of corneal defects. Eyes donated through the George Washington University Hospital will be preserved and flown by national airlines to the New York headquarters for examination and distribution well within the 48 hour "life" limit of the cornea.

ILLINOIS

Hospital News.—Ground was recently broken for the construction of a new annex to St. Francis Hospital in Evanston. A four story section will contain quarters for interns and resident physicians and a one story section an auditorium seating 400. The cost will be $351,000. The auditorium is being built as a memorial to Dr. Oscar T. Schultz, director of St. Francis Hospital pathologic laboratories from 1929 to 1943.

Chicago

Dr. Mead Wins Miller Award.—Dr. Arthur F. Mead has been awarded the 1950 Leo F. Miller Prize at the University of Illinois College of Medicine for his extensive study in the field of orthopedic surgery, entitled "Orthopaedic Implications of Fluorine." The prize carries a $50 stipend.

Faculty Research Award.—An annual faculty Meritorious Research Award of $250 has been established for the Chicago Medical School by an anonymous donor. The award will be given to a faculty member who is considered to have done the most outstanding research work in the year. Dr. Leo M. Zimmerman is chairman of the award committee.

Dr. Davis Appointed to Research Council.—Dr. Loyal Davis, Grunow professor of surgery and chairman of the department at the Northwestern University Medical School, was selected last month to represent the American College of Surgeons for three years in the Division of Medical Science on the National Research Council. Dr. Davis, also chief of staff of Surgical Division, Passavant Memorial Hospital, is a graduate of Knox College and Northwestern University Medical School (1918). He has been a member of the faculty since 1925 and chairman of the department of surgery since 1932.

IOWA

Town Fetes Physician.—Nearly 1,000 persons took part in a celebration honoring Dr. Harold A. Housholder of Winthrop. "Dr. Housholder Day" was celebrated with a parade, a picnic in the town park, band concerts and ball games. The doctor was presented checks totaling $900, which he turned over to the fund for the new wing of People's Hospital in Independence. Dr. Thomas F. Thornton of Waterloo spoke in behalf of the Iowa State Medical Society.

Cancer Institutes.—The Cancer Division of the Iowa State Department of Health will present cancer institutes in nine centers throughout the state this fall. Each institute will be a one day meeting consisting of four lectures, two before dinner and two after. The expenses and honorarium of the speakers are paid by the state department of health through the aid of federal funds made available to it for the purpose. The Iowa Division of the American Cancer Society is providing a complimentary dinner for attending physicians. The first institute will be held in Carroll September 7.

Medical-Press-Radio Conference. — Representatives of newspaper and radio stations in all sections of the state and a representative of each county society will attend the Iowa State Medical Society's second annual medical-radio-press conference at the Hotel Fort Des Moines in Des Moines September 8. Col. Elbert DeCoursey, army medical center, Washington, D. C., will speak on "Atomic Energy as It Relates to Medicine." Dr. John W. Ferguson, Newton, chairman of the state committee on emergency medical service, will make his report. Other subjects under discussion during the afternoon concern a grievance committee of the state society, placement of physicians in rural areas and advances in medical science. Representatives of the Iowa Radio News Editors Association, Iowa Press Association, Iowa State Medical Society and the State College radio station will discuss a code of cooperation. Discussion periods will be held. Mr. Thomas Hendricks, secretary of the Council on Medical Service, American Medical Association, Chicago, will speak on "Expansion of Voluntary Health Insurance."

KANSAS

Postgraduate Course in Anesthesiology.—A program for the postgraduate medical study of anesthesiology will be presented at the University of Kansas Medical School, Kansas City, September 18-20, with the cooperation of the Kansas City Society of Anesthesiologists, the Kansas Medical Society and the state board of health. Visiting speakers include Drs. Urban H. Eversole, Boston; Scott M. Smith, Salt Lake City; Lloyd H. Mousel, Seattle, and Donald L. Burdick, New York. The program has been designed to present subjects and problems which confront part time anesthesiologists. Requests for information may be directed to Dr. Paul H. Lorham, Department of Anesthesiology, University of Kansas Medical Center, Kansas City 3.

MARYLAND

Institute of Ministry to the Sick.—More than 60 Maryland clergymen of all denominations attended a two week institute on ministry to the sick held recently at Johns Hopkins Hospital, Baltimore. The institute, first of its kind held at Johns Hopkins, was designed to give clergymen a greater understanding of the many problems faced by hospital patients and their families and those of doctors, nurses and hospital authorities in administering treatment and care. This year's program was devoted exclusively to surgery and its related services, and it is planned to hold the institute annually covering a different branch each year. With the exception of the first day, which was given over to indoctrination and a tour of the hospital, each session was addressed by a member of the professional staff on a particular phase of surgery. The respective responsibilities of doctor and clergyman and how one can most effectively help the other in treating and consoling patients, the place of the hospital in the community and the problems faced in administering care to the largest number, and the role of the teaching hospital were among subjects discussed frankly and in detail at the sessions. Surgical services discussions included general surgery, anethesia, surgery of the genitourinary tract, eye surgery, children's surgery, orthopedic surgery, deafness, gynecology and autopsies.

MICHIGAN

Mental Hospital Unit.—A 650 bed unit of the Northville State Hospital is now under construction; it is to be ready for occupancy next spring. The unit is part of a master plan which will eventually give the hospital a capacity of 3,500 to 4,000 patients. The units now under construction are the 10 story medical section and adjoining two story administration section. A power plant and water system to serve the entire plan have been completed. These buildings have been constructed at a cost of $6,000,000. The legislature has also appropriated $287,000 for a building to house a staff and $80,000 to prepare plans for two additional buildings which will add 480 patient beds. Ultimate cost of the project will be about $20,000,000. This is the state's first hospital for the mentally ill to be built in 20 years.

Venereal Disease Control Programs.—To help offset the loss of the Rapid Treatment Center in Ann Arbor, the state Division of Venereal Disease Control has revamped its program, and members of the state health department are making a tour of all the local health departments to assist in expansion and correlation of local programs. The revamped venereal disease control program calls for assisting local health departments in intensified education programs, making available to local health departments venereal disease investigators to assist in contact-tracing and follow-up, providing for the services of private consultants who are specialists in syphilology and dermatology for diagnosis of problem cases and the distribution of penicillin to local health departments for use in clinics and to private physicians.

NEW JERSEY

Public Health Appointment.—Dr. Gorge F. Moench, health commissioner for Defiance County, Ohio, has been made director of the Division of Local Health Services in the state health department. His appointment completed the placement of division heads under reorganization authorized by the legislature a year ago. Dr. Moench, who has held various public health offices in midwestern and southern states, served as public health director of the Oak Ridge Tennessee Atomic Research Center before his Ohio appointment.

NEW MEXICO

Hospital News.—Ground breaking ceremonies for the new Las Vegas Community Hospital were conducted late in June. The structure is to be a 50 bed hospital to cost $543,647 and to be completed in 300 calendar days. It is being constructed with the aid of federal grants.

NEW YORK

Course in Treatment of Atomic Explosion Victims.—A postgraduate course in the diagnosis and emergency treatment of victims of atomic explosion will be made available to every doctor in New York State beginning in early September. Sessions will be conducted with the cooperation of the state medical schools, under the joint sponsorship of the state health department and the state medical society. Two instruction periods of three hours each have been arranged, during which lectures on shock, burns, fractures, wounds and radiation sickness will be given. The curriculum is being developed by a committee under the chairmanship of Dr. Joe W. Howland, chief, division of medical services of the atomic energy project at the University of Rochester School of Medicine and Dentistry.

Lay Nassau Hospital Cornerstone.—The cornerstone of a $10,000,000 addition to Nassau County's Meadowbrook Hospital was held July 23 in East Meadow, Long Island. The addition of 14 buildings to the original six will increase the hospital's capacity from 200 to 600 beds. Construction is expected to be completed in January 1952. The new buildings will include two for patients, a separate structure for the treatment of cancer patients and the chronically ill, an isolated unit in the pediatrics department for the care of 20 prematures, a laboratory and autopsy building, an administration building and two wings for the nurses' home. The x-ray department will be expanded to several times its present size. The entire operating department will be air conditioned and increased by four major operating rooms. A nursing unit of 26 beds in single rooms will be set aside for mental patients. A pneumatic tube system will connect most departments, and oxygen will be piped into all patient rooms. The nurses' home will be almost tripled.

New York City

Radium-Beam Therapy Unit.—The largest radium-beam therapy unit in the Western Hemisphere and the second largest in the world will be established this year at Roosevelt Hospital under the direction of Dr. Douglas Quick. Twenty-five grams of radium will be placed in a radium-beam therapy apparatus for the treatment of cancer in a special department of therapeutic radiology within the hospital. The department will be in operation before the end of 1950. The large amount of radium has been procured through the cooperation of the Union Miniere du Haut Katanga of Brussels, Belgium, and their American representatives, Radium Chemical Company, Inc. Gioacchino Failla, D.Sc., and Edith H. Quimby, Sc.D., director and associate director, respectively, of the Radiological Research Laboratory, Columbia University, will be the consulting physicists. The radium-beam therapy unit at Roosevelt will be located entirely underground. The department, including the beam room, examination rooms, physicists' laboratory and director's office, will be built in the area between the Russell Memorial Building and the site of the proposed Tower Memorial Building. The radiology department will be developed into a complete clinic or institute for the special clinical study and treatment of cancer by irradiation with particular reference to the use of gamma or radium radiation over its entire technical range of adaptability. Because of both the value and scarcity of such a large amount of radium, the department will operate on a 12 hour daily schedule in the beginning, gradually extending to continuous operation in order to treat more persons.

OHIO

Personal.—Dr. Ralph E. Dwork, a district health officer of New York City, has been appointed chief of the Division of Tuberculosis in the Ohio Department of Health. Dr. Dwork received his M.D. degree in Scotland in 1946 and has been engaged in tuberculosis hospital work at Otisville, N. Y., and in Denver.

Postgraduate Course in General Medicine.—On September 21-23 the Frank E. Bunts Institute and the Cleveland Clinic will present a continuation course for physicians on Practical Problems in General Medicine. Dr. Marion A. Blankenhorn, Helen Hughes Taylor professor of medicine at the University of Cincinnati College of Medicine, will give the evening address September 21 on "The Rickettsial Diseases." Other out-of-town guest speakers will be Dr. D. W. Pickering, director of the medical unit, St. Mary's Hospital, London, England, and Dr. E. Braun-Menendez of Buenos Aires, Argentina, who will speak on "Pathogenic Basis of the Treatment of Hypertension." Inquiries regarding the complete program and registration may be addressed to the Director of Education, Frank E. Bunts Educational Institute, 2020 East Ninety-Third Street, Cleveland 6.

SOUTH CAROLINA

Faculty Retirements.—At the end of the June session three members with long service on the faculty of the Medical College of the State of South Carolina, Charleston, retired as professors emeriti. Dr. George M. Mood, a graduate of the college in 1901, was professor of bacteriology and preventive medicine since 1913. He joined the staff in 1904. Dr. John F. Townsend, also an alumnus, had been associated with the college since 1907 and was made professor of ophthalmology, rhinology and otolaryngology in 1937. Dr. Daniel L. Maguire resigned as clinical professor of surgery. He joined the teaching staff following his graduation from the college in 1907. He had been clinical professor since 1944.

TEXAS

County Builds Hospital Without Federal Aid.—Ector County Hospital in Odessa has been built and paid for by the county without federal financial aid and without voluntary donations. The modern physical plant was built at a cost of $1,000,000. The medical staff of 22 doctors is headed by Dr. John K. Wood, Odessa.

Crosby Estate Student Loan Fund.—The Crosby Estate Student Loan Fund will be established according to the bequest of the late Mrs. Helene Simmons of Houston, widow of the late A. W. Crosby, oil millionaire. According to newspaper reports, the major portion of the estate, estimated to be $1,000,000 to $3,000,000, will go to Baylor University College of Medicine, Houston, for the loan fund.

Medical Branch Adds Physical Therapy Course.—A curriculum in physical therapy has been established at the University of Texas Medical Branch, Galveston, leading to a bachelor's degree. The course includes two years of general collegiate training with two years of special training. The curriculum is under the medical direction of Dr. G. W. N. Eggers, professor of orthopedic surgery.

UTAH

Nutritional Study of Rheumatic Fever Victims.—A study of the nutritional status of certain population groups in Utah is under way in the Ogden area by the Utah agricultural experiment station. This study is to determine relationships between diet and physical condition, dental health and constituents in the blood of normal and rheumatic fever children. Ethelwyn B. Wilcox, Ph.D., professor of nutrition, and Delbert A. Greenwood, Ph.D., professor of biochemistry, at the Utah State Agricultural College, have charge of the investigation. Cooperating agencies are the state department of health, the state medical and dental associations, Ogden City and Weber County commissions and health departments. Nutrition studies of approximately 150 who have rheumatic fever or who recently have had the disease will be made, and an equal number of normal children of similar age from the same economic levels will be studied in a like manner.

VERMONT

Dr. King Goes to Cleveland Clinic.—Dr. John W. King, associate professor of bacteriology and clinical pathology at the University of Vermont College of Medicine, Burlington, has joined the staff of Cleveland Clinic. He will head the department of clinical pathology. Dr. King is a graduate of Yale University School of Medicine, New Haven, Conn. (1944), and joined the faculty of the University of Vermont in 1946.

WEST VIRGINIA

Personals.—Dr. Everett L. Gage of Bluefield was reelected chairman of the West Virginia Section, Southeastern Surgical Congress, at the annual meeting held at White Sulphur Springs in July in conjunction with the sections of the congress from Virginia, Maryland and the District of Columbia.——Dr. James L. Patterson of Logan was reelected president of the West Virginia Chapter of the Medical College of Virginia Alumni Association at a meeting in July.

State Medical Election.—Dr. Frank J. Holroyd of Princeton was elected president of the West Virginia State Medical Association at the annual meeting at White Sulphur Springs, July 27-29. Drs. Alonzo R. Sidell of Williamstown was elected first vice president; Jacob C. Huffman of Buckhannon, second vice president, and T. Maxfield Barber of Charleston, treasurer. Dr. Walter E. Vest of Huntington was reelected delegate to the American Medical Association and Dr. Pat A. Tuckwiller of Charleston alternate.

WISCONSIN

Physicians Prepare Medical Cival Defense System.—Thirty-one out of 52 county medical societies in the state have operating committees for providing medical care in the event of an emergency, according to Dr. Frank L. Weston, Madison, chairman of the state medical society's committee of military medical service. At a meetinge July 5 the committee completed detailed plans for the organization of disaster units in every county. State medical society plans will be integrated with those already established in many cities. The society is working in cooperation with the Wisconsin National Guard and the Adjutant General's Office, the Red Cross, the state board of health and members of other health professions. The units include a collection team to go immediately to the scene of the disaster and screen casualties, a first aid team, an ambulance team and surgical medical teams.

GENERAL

Society Election.—At the annual meeting of the American Proctologic Society in Los Angeles July 2-5 the following officers were elected: Drs. Hoyt R. Allen, Little Rock, Ark., president; Robert A. Scarborough, San Francisco, president-elect; W. Wendell Green, Toledo, Ohio, secretary, and Rufus C. Alley, Lexington, Ky., treasurer.

Grants for Ophthalmologic Research.—The National Council to Combat Blindness, Inc., is accepting requests for grants in aid of ophthalmologic research for the period July 1951 to June 1952. Applications should be in the office of the council no later than March 1, 1951. Appropriate forms may be obtained by writing the Secretary, National Council to Combat Blindness, Inc., 1186 Broadway, New York 1.

Nutrition Symposium.—A medical symposium on the Biological Significance of Lipids will be held September 13 and 14 at the University of Rochester (N. Y.) School of Medicine and Dentistry. It is the third in an annual nutrition series sponsored by the Robert Gould Foundation, Cincinnati. Invitations to the conference have been sent to scientists in this country and Canada and abroad. The sessions will honor Walter R. Bloor, Ph.D., professor emeritus of biochemistry at the medical school.

Research Awards of Memorial Fund.—The Jane Coffin Childs Memorial Fund for Medical Research announced July 1 appropriations made by its board of managers on Nov. 18, 1949, February 17 and June 5 in a total sum of $171,375 for support of cancer research projects and fellowships. The 21 grants included seven to Yale University personnel and four to foreign research workers. Among the largest grants were:

Francisco Duran-Reynals, Yale University, New Haven, Conn., $49,500 for three years for continued study of the part played by viruses in the genesis of cancer.

Balduin Lucke, University of Pennsylvania, Philadelphia, $20,400 for three years for studies on enzyme patterns in relation to development and growth of neoplasms and on the mechanism of metastasis.

William U. Gardner, Ph.D., Yale University, $18,000 for three years for investigations on the role of hormones in normal and abnormal growth.

Leonell C. Strong, Ph.D., Yale University, $13,430 for one year for genetic studies on the induction of tumors by methylcholanthrene.

Dr. John C. Sonne, fellow, University of Pennsylvania, $8,000 for two years.

Eugene L. Opie, Rockefeller Institute for Medical Research, New York, $8,000 for one year for studies on osmotic and cytologic effects of hepatic-tumor-producing diets.

Grants for Environmental Cancer Research.—The Committee on Growth of the National Research Council, adviser for research to the American Cancer Society, announces the formation of a Panel on Environmental Cancer with the following membership: Dr. Willard F. Machle, New York, chairman; Dr. Francis F. Heyroth, Cincinnati; Dr. George H. Gehrmann, Wilmington, Del.; Dr. Hermann Lisco, Chicago, and Norton Nelson, Ph.D., New York. Increasing realization of the importance of further research in environmental cancer led to the creation of this new panel, which, at the outset, will concern itself with an evaluation of the status of knowledge in this field and with the formulation of criteria for the establishment of valid relationships between environment and occupation and the occurrence of cancer. The panel also will review applications for grants in support of research in these areas. These applications, as with others submitted to the Committee on Growth, will be received until October 1. Communications regarding grants may be addressed to the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Avenue, N. W., Washington 25, D. C.

New Boundaries for Yellow Fever Zones.—A revised delineation of the two zones of prevalence of the yellow fever virus in tropical belts of the Americas and of Africa is published in the World Health Organization's *Weekly Epidemiological Record* for June 28. The revision was drawn up by a WHO panel of experts last December and accepted at the Third World Health Assembly in May. According to international sanitary agreements, countries are required to take special quarantine measures against persons and transport coming from or going to the zones concerned. The endemic yellow fever area in Africa is limited in the north by a line from the mouth of the Senegal River in French West Africa to Eritree (excluding the port of Massawa) and extends southward to the tenth degree of latitude enclosing part of Angola in the west, the major part of the Belgian Congo and all of Kenya in the east. Djibuti and the rest of French Somaliland were excluded from the endemic area by the December 1949 revision, while parts of Bechuanaland and all of Nyassaland were added to it. Modifications result partly from surveys on the occurrence of the disease and partly from the results of anti-aegypti measures in urban communities. In the Americas the endemic zone comprises Venezuela, Colombia, the British, Dutch and French Guianas and parts of Brazil, Peru, Bolivia and Ecuador but excludes certain northern ports.

Grants for Heart Research Available.—The American Heart Association has announced that new applications for research fellowships and established investigators will be accepted until September 15. Applications for research grants, including grants to basic sciences, may be filed up to December 15. Information and application forms may be obtained from Dr. Charles A. R. Connor, Medical Director, American Heart Association, 1775 Broadway, New York 19. Ten per cent of the association's research funds, or about $45,000, will be available during the academic year 1951-1952 to support research investigations in basic sciences, even though such investigations are not directly related to the field of cardiovascular diseases.

Fellowships for established investigators may be granted for a five year period at a minimum stipend of $5,000, with an annual increase of $500. They are open to persons of superior qualification and proved originality with M.D., Ph.D. or Sc.D. degrees or their equivalent, who are interested in making a career of research (THE JOURNAL, June 24, p. 754).

Research fellowships are granted for a one year period with a stipend ranging from $3,000 to $4,300. They are open to graduates of approved medical or graduate schools who are interested in research and intend to follow an academic career. Grants in aid are available to nonprofit institutions possessing the requisite basic facilities for research and having the necessary experienced investigators on their staffs. They are designated for a specified program of research. It is estimated that more than $1,000,000, or over 25 per cent of the $4,000,000 raised nationally during the 1950 Heart Campaign, will have been allotted this year to research support of all kinds by the association and its affiliates. Of this total about $450,000 represents funds of the national association.

Prevalence of Poliomyelitis.—Reports of cases of poliomyelitis for the periods indicated have been received from the National Office of Vital Statistics, U. S. Public Health Service.

	Week Ended		Total*		5-Year
	Aug. 5, 1950	Aug. 6, 1949	1950	1949	Median, 1945-1949
United States Total	1,186	2,446	6,171	9,810	4,983
New England States:					
Maine	1	21	13	84	5
New Hampshire	..	9	8	18	10
Vermont	..	7	4	11	6
Massachusetts	9	82	37	215	26
Rhode Island	2	7	8	14	1
Connecticut	7	32	43	78	29
Middle Atlantic States:					
New York	95	390	412	842	219
New Jersey	24	81	133	178	128
Pennsylvania	49	29	137	84	78
East North Central States:					
Ohio	44	99	153	249	140
Indiana	14	96	48	360	43
Illinois	77	250	260	583	163
Michigan	41	145	174	447	79
Wisconsin	23	53	85	158	58
West North Central States:					
Minnesota	13	94	57	411	146
Iowa	46	84	237	279	114
Missouri	15	110	79	464	57
North Dakota	1	48	3	125	18
South Dakota	2	14	16	78	46
Nebraska	19	31	101	115	107
Kansas	29	46	90	225	70
South Atlantic States:					
Delaware	1	3	7	12	7
Maryland	11	14	30	32	17
District of Columbia	15	4	50	16	16
Virginia	88	27	319	72	72
West Virginia	19	26	78	111	17
North Carolina	41	11	145	82	41
South Carolina	26	1	193	28	28
Georgia	31	13	82	70	56
Florida	12	8	97	78	78
East South Central States:					
Kentucky	42	35	182	177	40
Tennessee	45	36	143	199	102
Alabama	12	6	111	106	80
Mississippi	18	22	133	143	50
West South Central States:					
Arkansas	11	63	112	539	57
Louisiana	29	4	126	88	51
Oklahoma	35	75	208	589	125
Texas	122	121	1,271	1,233	519
Mountain States:					
Montana	3	5	10	15	12
Idaho	2	33	22	146	19
Wyoming	3	9	19	25	19
Colorado	7	33	45	108	25
New Mexico	6	11	31	59	25
Arizona	2	6	37	33	29
Utah	2	8	11	52	21
Nevada	..	2	1	10	1
Pacific States:					
Washington	9	24	57	98	56
Oregon	7	6	51	58	21
California	76	112	507	618	324

* Beginning with the 12th week of each year.

Red Cross Accepts Request to Collect Blood.—General George C. Marshall, president of the American Red Cross, has accepted a request by Secretary of the Defense Louis Johnson that the Red Cross become the official agency for the procurement of blood for the armed forces when such blood and its derivatives are needed. Secretary Johnson recommended that a relationship between the American Red Cross and the Department of Defense be established simliar to that which existed during World War II, so that in time of need the armed forces may look to the Red Cross as the official whole blood and blood derivatives procurement agency. General Marshall designated Vice Admiral Ross T. McIntire (MC, USN), retired, of the Red Cross National Blood Program, to work with Dr. Richard L. Meiling, director of medical services of the Department of Defense, to coordinate and develop the plan. At present 34 regional blood centers and 46 mobile units are operating in the Red Cross blood program. They are now collecting approximately 63,200 pints of blood a month for civilian use. A total of 677 Red Cross chapters are participating in the collection and processing centers. The regional centers are serving more than 1,900 hospitals in 38 states and are so established that they can be swung immediately into action in event of a national emergency. Since the inauguration of the postwar National Blood Program of the Red Cross in January 1948, about 844,160 pints of whole blood have been processed and distributed to hospitals, physicians and clinics. Regional blood centers of the Red Cross National Blood Program are now in operation at Rochester, N. Y.; Wichita, Kan.; Stockton, Calif.; Atlanta, Ga.; Boston; Washington, D. C.; Los Angeles; Tucson, Ariz.; San Jose, Calif.; Omaha; Springfield, Mo.; St. Louis; Charlotte, N. C.; Lansing, Mich.; Detroit; Yakima, Wash.; Great Falls, Mont.; Columbus, Ohio; St. Paul; Nashville, Tenn.; Portland, Ore.; Boise, Idaho; Philadelphia; Asheville, N. C.; Louisville, Ky.; Syracuse, N. Y.; Mobile, Ala.; Johnstown, Pa.; Savannah, Ga.; Norfolk, Va.; Wilkes-Barre, Pa.; Buffalo; Hartford, Conn., and Madison, Wis.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Chicago, Oct. 8-11. Sec., Dr. Curtiss B. Hickcox, 745 Fifth Ave., New York 22.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written.* Various locations, Sept. 14. *Oral.* Detroit, Oct. 20-22. Sec., Dr. George M. Lewis, 66 East 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 16. Asst. Sec., Dr. William A. Werrell, 1 West Main Street, Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 1950. Applications no longer accepted. Sec., Dr. W. J. German, 789 Howard Ave., New Haven, Conn.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral, including sub-specialties,* Oct. 26-28. Final date for filing application was August 19. *Oral, including sub-specialties,* Dec. 7-9. Executive Secretary-Treasurer, Dr. William A. Werrell, 1 West Main St., Madison 3.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers. Jan. 5-6, 1951. San Francisco, March 11-15; New York, May 31-June 4. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 25-26. Final date for filing applications is Aug. 15, 1950. Sec., Dr. Harold A. Sofield, 122 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 3-6. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PATHOLOGY: St. Louis, Oct. 13-14. Sec., Dr. Robert R. Moore, 507 Euclid Ave., St. Louis 10.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 13-15 and Boston, Dec. 1-3. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Oral and Written.* Boston, Aug. 26-27. Final date for filing applications is April 1. Sec., Dr. Robert L. Bennett, 30 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PLASTIC SURGERY: Houston, Nov. 30, Dec. 1-2. Sec., Dr. Bradford Cannon, 4647 Pershing Ave., St. Louis.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: St. Louis, Oct. 28-29. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Next examination, Dec. 18-19. Final date for filing applications is Sept. 1.

AMERICAN BOARD OF RADIOLOGY: Chicago, Dec. 5-10. Quota of appointments already filled. Sec., Dr. B. R. Kirklin, Mayo Clinic, Rochester.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers, Oct. 25. *Written.* Various centers, March 1951. Final date for filing applications is Dec. 1, 1950. Sec., Dr. J. Stewart Rodman, 225 South 15th Street, Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 10-14, 1951. Final date for filing applications is Sept. 1, 1950. Sec., Dr. Harry Culver, 7935 Sunnyside Road, Minneapolis 21.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 26-28. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery.

ALASKA: Juneau, Sept. 5. Special examinations given on application Sec., Dr. W. M. Whitehead, Box 140, Juneau.

ARKANSAS: * Little Rock, Nov. 9-10. Sec., Dr. Joe Verser, Harrisburg. Homeopathic: Nov. Sec., Dr. C. S. Bungart, 105 N. 14th St., Ft. Smith.
COLORADO: * Denver, Jan. 3-5, 1951. Exec. Sec., Mrs. B. M. Hudgens, 831 Republic Bldg., Denver.
CONNECTICUT: * Hartford, Nov. 14-15. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven. Homeopathic: Nov. 14-15. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.
DELAWARE: Dover, Jan. 9, 1951. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.
DISTRICT OF COLUMBIA: * Washington, Sept. 18. Sec., Dr. Daniel L. Seckinger, 4130 Municipal Bldg., Washington.
FLORIDA: * Jacksonville, Nov. 26-28. Sec., Dr. Homer Pearson, 701 Dupont Bldg., Miami.
GEORGIA: Atlanta, Oct. 10-11. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta 3.
HAWAII: Honolulu, Jan. 8-11, 1951. Sec., Dr. I. L. Tilden, 881 S. Hotel St., Honolulu.
ILLINOIS: Chicago, Oct. 10-12. Superintendent of Registration, Mr. Charles F. Kervin, Capitol Bldg., Springfield.
INDIANA: Indianapolis, June 1951. Exec. Sec., Miss Ruth V. Kirk, 1138 K. of P. Bldg., Indianapolis 4.
IOWA: *Written.* Des Moines, Dec. 4-6. Acting Director, Division of Examination and Licensure, State Department of Health, 1027 Des Moines St., Des Moines.
KANSAS: Topeka, Dec. 13-14. Sec., Dr. O. W. Davidson, 772 New Brotherhood Bldg., Kansas City.
LOUISIANA: New Orleans, Dec. 8-10. Sec., Dr. R. B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.
MAINE: Portland, Nov. 14-15. Sec., Dr. Adam P. Leighton, 192 State St., Portland.
MARYLAND: Baltimore, Dec. 12-15. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1.
MASSACHUSETTS: Boston, Jan. 23-26, 1951. Sec., Dr. Geo. R. Schadt, 37 State House, Boston.
MINNESOTA: * Minneapolis, Oct. 17-19. Sec., Dr. J. F. Du Bois, 230 Lowry Medical Arts Bldg., St. Paul 2.
MISSISSIPPI: Jackson, December. Asst. Sect., Dr. R. N. Whitfield, Jackson 113.
MONTANA: Helena, Oct. 2. Sec., Dr. S. A. Cooney, 7 W. 6th Ave., Helena.
NEBRASKA: * June 1951. Director, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln.
NEVADA: Carson City, August 7. Sec., Dr. G. H. Ross, 112 N. Curry St., Carson City.
NEW HAMPSHIRE: Concord, Sept. 13. Sec., Dr. John Samuel Wheeler, 107 State House, Concord.
NEW JERSEY: Trenton, Oct. 17-20. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.
NEW MEXICO: * Santa Fe, Oct. 9-10. Sec., Dr. Charles J. McGoey, Coronado Building, Santa Fe.
NEW YORK: New York, Buffalo, Albany and Syracuse, Oct. 3-6. Sec., Dr. Jacob L. Lochner, 23 S. Pearl St., Albany.
NORTH CAROLINA: *Reciprocity.* Raleigh, Sept. 25. Sec., Dr. Ivan Procter, 226 Hillsboro St., Raleigh.
NORTH DAKOTA: Grand Forks, Jan. 3-6. Sec., Dr. C. J. Glaspel, Grafton.
OHIO: Columbus, December. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.
PENNSYLVANIA: Philadelphia, January 1951. Acting Secretary, Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.
PUERTO RICO: *Examination.* Santurce, Sept. 5-9. Sec., Mr. Luis Cueto, Coll. Box 3717, Santurce.
RHODE ISLAND: * Providence, Oct. 5-6. Chief, Mr. Thomas B. Casey, 355 State Office Bldg., Providence.
SOUTH CAROLINA: Columbia, Nov. 13-15. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.
TENNESSEE: * Memphis, Sept. 27-28. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis 3.
TEXAS: * Fort Worth, November 1950. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth.
UTAH: Salt Lake City, July 1951. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.
VERMONT: Burlington, February 1951. Sec., Dr. F. J. Lawliss, Richford.
WASHINGTON: * Seattle, January 1951. Sec., Mr. Edward C. Dohm, Department of Licenses, Olympia.
WEST VIRGINIA: Charleston, Oct. 2-4. Sec., Dr. N. H. Dyer, State Capitol, Charleston 6.
WISCONSIN: * River Falls, Jan. 9-11, 1951. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.
WYOMING: Cheyenne, Oct. 2. Sec., Dr. Franklin D. Yoder, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* Juneau, last week in August. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.
ARIZONA: Tucson, Sept. 19. Sec., Mr. Francis A. Roy, Science Hall, Univ. of Arizona, Tucson.
ARKANSAS: Little Rock, Oct. 3-4. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.
COLORADO: *Examination.* Denver, Sept. 13-14. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 3.
CONNECTICUT: Oct. 14. Executive Sec., M. G. Reynolds, State Board of Healing Arts, 110 Whitney Ave., New Haven 10.
DISTRICT OF COLUMBIA: Washington, Oct. 23-24. Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.
FLORIDA: Jacksonville, Nov. 11. Sec., Mr. M. W. Emmel, University of Florida, Gainesville.
IOWA: Des Moines, Oct. 10. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.
MICHIGAN: *Examination.* Ann Arbor, Oct. 13-14. Sec., Miss Eloise LeBeau, 101 North Walnut Street, Lansing 15.
MINNESOTA: Minneapolis, Oct. 3-4. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14.
NEBRASKA: *Examination.* Omaha, Oct. 3-4. Director, Mr. Oscar F. Humble, Room 1009, State Capitol Building, Lincoln 9.
NEW MEXICO: *Examination.* Santa Fe, Sept. 17. Sec., Mrs. Marguerite K. Cantrell, Box 1522, Santa Fe.
OKLAHOMA: *Examination.* Oklahoma City, Sept. 15. Sec., Dr. Clinton Gallaher, 813 Braniff Building, Oklahoma City.
OREGON: *Examination.* Portland, Sept. 9. Sec., Dr. C. D. Byrne, University of Oregon, Eugene.
RHODE ISLAND: *Examination.* Providence, Nov. 8. Chief, Division of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Building, Providence.
SOUTH DAKOTA: Vermillion, Dec. 1-2. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.
TENNESSEE: Memphis, Sept. 21-22. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis 3.
TEXAS: *Examination.* Austin, October. Sec., Brother Raphael Wilson, 306 Nalle Building, Austin.
WASHINGTON: Seattle, January 1951. Sec., Mr. Edward D. Dohm, Department of Licenses, Olympia.
WISCONSIN: *Examination.* Milwaukee, Dec. 2. Sec., Mr. W. H. Barber, Scott and Watson Sts., Ripon.

Coming Medical Meetings

American Academy of Ophthalmology and Otolaryngology, Palmer House, Chicago, Oct. 8-13. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.
American Association of Obstetricians, Gynecologists and Abdominal Surgeons, The Homestead, Hot Springs, Va., Sept. 7-9. Dr. Leroy A. Calkins, University of Kansas Medical Center, Kansas City 3, Secretary.
American Congress of Physical Medicine, Boston, Aug. 29-Sept. 1. Dr. Richard Kovacs, 2 E. 88th St., New York City 28, Secretary.
American Hospital Association, Atlantic City, Sept. 18-22. Mr. George Bugbee, 18 E. Division St., Chicago 10, Executive Director.
Biological Photographic Association, Hotel Sheraton, Chicago, Sept. 6-8. Mr. Lloyd E. Varden, Pavelle Color, Inc., 533 W. 57th St., New York City 19, Secretary.
Colorado State Medical Society, Broadmoor Hotel, Colorado Springs, Sept. 20-23. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver 2, Executive Secretary.
Delaware, Medical Society of, Dover, Oct. 2-4. Dr. Andrew H. Gehret, 1007 Park Place, Wilmington, Secretary.
District of Columbia, Medical Society of the, Washington, Oct. 2-4. Mr. Theodore Wiprud, 1718 M Street N.W., Washington 6, Secretary.
Idaho State Medical Association, Sun Valley, Sept. 6-9. Dr. Alfred M. Popma, 220 N. First St., Boise, Secretary.
Indiana State Medical Association, French Lick, Sept. 25-27. Mr. Ray E. Smith, 23 E. Ohio St., Indianapolis 4, Executive Secretary.
Kentucky State Medical Association, Brown Hotel, Louisville, Sept. 26-28. Dr. Bruce Underwood, 620 S. Third St., Louisville 2, Secretary.
Michigan State Medical Society, Book-Cadillac Hotel, Detroit, Sept. 20-22. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing 8, Secretary.
Mississippi Valley Medical Society, Springfield, Ill., Sept. 27-29. Dr. Harold Swanberg, 510 Maine St., Quincy Ill., Secretary.
National Medical Association, Hampton Institute, Hampton, Va., Aug. 28-Sept. 1. Dr. John T. Givens, 1108 Church St., Norfolk 10, Va., General Secretary.
Nevada State Medical Association, Las Vegas, Oct. 5-7. Dr. Wesley W. Hall, 307 West Sixth St., Reno, Secretary.
New Hampshire Medical Society, Mt. Washington Hotel, Bretton Woods, Sept. 10-12. Dr. Deering G. Smith, 44 Chester St., Nashua, Secretary.
Oregon State Medical Society, Gearhart, Sept. 27-29. Dr. Werner E. Zeller, Medical-Dental Bldg., Portland 5, Secretary.
Southwestern Surgical Congress, Shirley-Savoy Hotel, Denver, Colo., Sept. 25-27. Dr. C. R. Rountree, 525 N.W. Eleventh St., Oklahoma City, Secretary.
Vermont State Medical Society, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 10-12. Dr. James P. Hammond, 128 Merchants Row, Rutland, Secretary.
Virginia, Medical Society of, Roanoke, Oct. 8-11. Mr. H. S. Johnson, 1200 East Clay St., Richmond 19, Executive Secretary.
Washington State Medical Association, Davenport Hotel, Spokane, Sept. 10-13. Dr. James W. Haviland, 338 White-Henry-Stuart Bldg., Seattle, Secretary.
Wyoming State Medical Society, Cody, Sept. 7-9. Dr. George H. Phelps, 1604 Capitol Ave., Cheyenne, Secretary.

International Meetings

International Conference of Speech and Voice Therapy, Amsterdam, Holland, Aug. 21-26. Dr. Deso A. Weiss, 106 E. 85th St., New York City 28, Secretary.
International Congress on Cardiology, Paris, France, Sept. 3-9. Dr. Mouquin, 78 rue de l'Abbé-Groult, Paris 15e, France, Secretary-General.
International Congress on Criminology, Palais de la Sorbonne Grand Amphitheater, Paris, France, Sept. 10-19. M. Pierre Piprot d'Alleaume, 188 Ave. Victor Hugo, Paris 16e, France, General Secretary.
International Congress on Diseases of the Chest, Carlo Forlanini Institute, Rome, Italy, Sept. 17-22. Prof. A. Omodei Zorini, Carlo Forlanini Institute, Rome, Italy, Chairman.
International Congress of Experimental Cytology, New Haven, Conn., U. S. A., Sept. 4-8. Dr. Danielli, King's College, London, England, Secretary.
International Congress on Internal Medicine, Paris, France, Sept. 11-14. Prof. Justin Besancon, 38 rue Barbet de Jouy, Paris, France, Secretary.
International Congress of Microbiology, Rio de Janeiro, Brazil, Aug. 17-24. Dr. Olympio de Fonseca, Institut Oswaldo Cruz, Rio de Janeiro, Secretary.
International Congress of Psychiatry, Palais de la Sorbonne, Paris, France, Sept. 19-27. Dr. Henri Ey, 1 rue Cabanis, Paris 14e, France, General Secretary.
International Society for the History of Medicine, Amsterdam, Holland, Aug. 14-20. Professor Guiart, 58 Blvd. de la Croix Rousse, Lyon, France, Secretary.
International Society for Internal Medicine, Paris, France, Sept. 11-15. Dr. Albert M. Snell, 102 Second Ave. S.W., Rochester, Minn., Chairman, American Committee.
International Union Against Tuberculosis, Copenhagen, Denmark, Sept. 1-8. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary.
Medical Women's International Association, Philadelphia, Penna., U. S. A., Sept. 10-16. Dr. Montreuil-Straus, 75 rue de l'Assomption, Paris, France, Secretary.
World Federation for Mental Health, Cité Universitaire, Paris, France, Aug. 31-Sept. 7. Secretary, 19 Manchester St., London, W.1, England.

DEATHS

Burlingame, C. Charles ✦ Hartford, Conn.; psychiatrist-in-chief of the Neuro-Psychiatric Institute of Hartford Retreat, now the Institute of Living, of which he was president and chairman of the board of managers, died in a private hospital in Leicester, England, July 22, aged 64. Dr. Burlingame was born in Rockford, Ill., Oct. 27, 1885. He received his medical degree from the Hahnemann Medical College and Hospital, Chicago, 1908. He was assistant physician at Westboro (Mass.) State Hospital and from 1912 to 1915 medical director, assistant superintendent and acting superintendent of Fergus Falls (Minn.) State Hospital. Dr. Burlingame was industrial psychiatrist of Cheney Brothers in Manchester, Conn., from 1915 to 1917 and from 1919 to 1921. He was interested in the application of psychiatric principles to industrial management and served as chairman of the subcommittee on psychiatry for the National Association of Manufacturers and other industrial medical organizations. During World War I he became a lieutenant colonel of the U. S. Medical Corps of the American Expeditionary Forces; as director of the Medical and Surgical Section, Department of Military Affairs, Bureau of Hospital Administration, and director of the Medical and Surgical Department of the American Red Cross in France. During World War II he served as expert consultant in psychiatry to the Secretary of War, attached to the Inspector General's Office, General Staff, U. S. Army. Both during and after the war Dr. Burlingame was consultant to selective service boards, veterans boards and the permanent armed forces training programs. From 1936 to 1938 he was clinical professor of psychiatry and mental hygiene at Yale University School of Medicine in New Haven.

A specialist certified by the American Board of Psychiatry and Neurology, Dr. Burlingame was chairman of the Salmon Committee on Psychiatry and Mental Hygiene of the New York Academy of Medicine, director of the Psychiatric Foundation; a life member of the American Psychiatric Association, chairman of that organization's section on mental hospitals, a member of its Central Inspection Board and its director of publicity in the U. S. for the International Congress of Psychiatry, on the governing board of the International Committee for Mental Hygiene, a member of the American Society of Research on Psychosomatic Problems, American Psychosomatic Society, Southern Psychiatric Association, New England Society of Psychiatry, Association for Research in Nervous and Mental Diseases, New York Psychiatric Association, New York Neurological Society, New York Society of Clinical Psychiatry, Connecticut Society of Psychiatry, Connecticut Society of Mental Hygiene, of which he had been vice president from 1938 to 1940, and the American Academy of Psychiatry, of which he was secretary-treasurer. He was a life member of the American College of Physicians and American Hospital Association, a member of the Association for the Study of Internal Secretions, American Association of Industrial Physicians and Surgeons, the Pan American Medical Association, World Medical Association and Hartford Medical Society, of which he had been president. In 1950 Dr. Burlingame became president-elect of the Connecticut State Medical Society, after having served on its council and on many committees. He was an honorary member of the Sociedad Mexicana de Eugenesia, and a corresponding member of the Sociedad Cubana de Neurologia y Psiquiatria.

From 1921 to 1928 Dr. Burlingame was executive officer of the joint administrative board of Columbia-Presbyterian Medical Center in New York, where from 1923 to 1935 he was executive vice president of Presbyterian Hospital. He was attending neuropsychiatrist, Veterans Home and Hospital Commission of Connecticut, associate attending psychiatrist, Vanderbilt Clinic, New York, consultant in psychiatry to U. S. Veterans Hospital in Newington, Hartford and St. Francis hospitals in Hartford, Charlotte Hungerford Hospital in Torrington, Hospital of St. Raphael in New Haven and the Meriden (Conn.) Hospital. After service for a number of years as senior consultant to the U. S. Veterans Hospital in Northampton, Mass., he was recently made chairman of the dean's committee there. He was also a member of the courtesy staff of the Neurological Institute in New York. Dr. Burlingame spent many years in psychiatric service of state hospitals in Massachusetts and Minnesota and was chairman of the Advisory Board in America of the American Hospital in Paris. Since 1925 he was hospital consultant to the governments of Uruguay and other South American and European countries. Since 1932 he was associate in psychiatry at Columbia University College of Physicians and Surgeons in New York. Had he lived, he would have headed the Section on Psychosurgery and Rehabilitation for the International Congress of Psychiatry in Paris in September. He was decorated by France, Poland and Czechoslovakia and received a citation for conspicuous and meritorious service with the American Expeditionary Forces. His public service activities included service as honorary consultant psychiatrist to the New York Police Department; chairmanship of the committee to govern licensing of practicing psychologists for the Connecticut Board of Education, and various other commissions and committees for the improvement of care of mental defectives and the mentally ill. He was an honorary member of the Royal Medico-Psychological Association, whose meeting he was attending at the time of his death, as a delegate of the American Psychiatric Association. Dr. Burlingame had been editor of the *Digest of Neurology and Psychiatry* and associate editor of the *American Journal of Psychiatry*.

Ryan, Maxwell Donnell ✦ New York; born in Leavenworth, Kan., July 20, 1901; McGill University Faculty of Medicine, Montreal, Canada, 1927; clinical professor of otorhinolaryngology at New York University College of Medicine; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and American Laryngological, Rhinological and Otological Society; fellow of the American College of Chest Physicians; affiliated with the New York Eye and Ear Infirmary and St. Clare's Hospital; consulting bronchoscopist at Pilgrim State Hospital, Brentwood, N. Y., and Kings Park (N. Y.) State Hospital; consulting surgeon, National Hospital for Speech Disorders; died June 11, aged 49, of heart disease.

Lund, Fred Bates, Newton, Mass.; born in Concord, N. H., Jan. 4, 1865; Harvard Medical School, Boston, 1892; formerly on the faculty of his alma mater; member of the American Medical Association, serving as a member of its House of Delegates in 1907, 1914, 1916-1917, 1920, 1922-1924, 1926-1928; member of the American Surgical Association, Society of Clinical Surgery, of which he had been president, and New England Surgical Society; fellow of the American College of Surgeons; served during World War I; for many years associated with Boston City, New England Deaconess and Carney hospitals in Boston; author of a book entitled "Greek Medicine"; died June 22, aged 85.

Geer, Everett Kinne ✦ St. Paul; born in St. Paul, 1893; University of Minnesota Medical School, Minneapolis, 1917; assistant professor of medicine at his alma mater; specialist certified by the American Board of Internal Medicine; member of the Central Society for Clinical Research, National Tuberculosis Association and American Trudeau Society; served during World War I; area consultant in the tuberculosis branch, Veterans Administration; fellow of the American College of Physicians; affiliated with Ancker Hospital, Children's Preventorium of Ramsey County and Bethesda, Charles T. Miller, St. Joseph's and St. Luke's hospitals; died May 3, aged 57, of coronary thrombosis.

Thomson, Alec Nicol ✦ Cutchogue, N. Y.; born in East Orange, N. J., Sept. 8, 1881; Long Island College Hospital, Brooklyn, 1905; formerly on the faculty of his alma mater; fellow of the American Public Health Association; at one time director of medical activities for the Kings County Medical Society and medical director of the American Social Hygiene Association; served during World War I; formerly practiced in Brooklyn, where he was on the staffs of Swedish and Brooklyn hospitals; administrator of the Eastern Long Island Hospital in Greenport; died in Bellevue Hospital, New York, July 4, aged 68, of coronary disease.

Berg, Albert Ashton ✦ New York; born in New York in 1873; College of Physicians and Surgeons, medical department of Columbia College, New York, 1894; past president of the International College of Surgeons; member of the American Gastro-Enterological Association; formerly professor of surgery at his alma mater; trustee of the New York Public Library; affiliated with Barnet Memorial Hospital, Paterson, N. J., Monmouth Memorial Hospital in Long Branch, Beth Moses Hospital in Brooklyn, Hebrew Orphan Asylum, Montefiore Hospital, Sydenham Hospital and Mount Sinai Hospital, where he died July 1, aged 77, after an operation on the kidney.

Beers, Nathan Thomas ✦ Brooklyn; born in Brooklyn March 29, 1874; Long Island College Hospital, Brooklyn, 1897; specialist certified by the American Board of Dermatology and

Syphilology; member of the American Radium Society; fellow of the American College of Physicians; veteran of the Spanish-American War and World War I; consulting dermatologist for the New York City Police Department; affiliated with Brooklyn, Carson C. Peck Memorial, Methodist, St. John's and St. Mary's hospitals; died in Fitkin Memorial Hospital, Neptune, N. J., July 7, aged 76, of thrombosis of the meningeal artery.

Cardle, Archibald Evans ✠ Minneapolis; born in El Reno, Okla., April 27, 1899; State University of Iowa College of Medicine, Iowa City, 1923; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past president of the Minnesota State Medical Association; in June 1948 received the Minneapolis Star and Tribune Award for leadership in Minnesota; on the faculty of the University of Minnesota Medical School; affiliated with Asbury, Northwestern and Abbott hospitals; died June 24, aged 51, aboard a plane that fell into Lake Michigan.

Beam, Hugh Martin ✠ Roxboro, N. C.; Columbia University College of Physicians and Surgeons, New York, 1918; past president of the Person County Medical Society; served as county health officer; during World War II was a member of the Selective Service Board of North Carolina; died in Duke Hospital, Durham, June 9, aged 59, of mesenteric thrombosis.

Bingham, William Otto, Elizabethton, Tenn.; Tennessee Medical College, Knoxville, 1909; formerly health officer of Carter County; died May 23, aged 66.

Blatz, Valentin, Oconomowoc, Wis.; St. Louis University School of Medicine, 1946; died in St. Joseph's Hospital, Milwaukee, May 5, aged 30, of multiple sclerosis.

Burt, Charles Thomas, Meridian, Miss.; University of Tennessee College of Medicine, Memphis, 1914; member of the American Medical Association; for many years health officer of the city of Meridian; died in Rush Memorial Hospital May 26, aged 78, of cerebral hemorrhage.

Campbell, John Lee, Ben Hill, Ga.; Atlanta Medical College, 1896; died April 16, aged 78.

Carlson, Benjamin, Lorain, Ohio; Western Reserve University Medical School, Cleveland, 1925; member of the American Medical Association; past president of the Lorain County Medical Society; served during World War I; formerly on the board of directors of Pleasant View Sanatorium in Amherst; at one time affiliated with St. Joseph's Hospital; died June 16, aged 57.

Cloyd, Augustus Davis ✠ Omaha; Missouri Medical College, St. Louis, 1886; an Associate Fellow of the American Medical Association; served as medical director of the Woodmen of the World and as acting superintendent of the Woodmen of the World War Memorial Hospital in San Antonio, Texas; died May 16, aged 90.

Conrad, Belle H., Seattle; State University of Iowa College of Medicine, Iowa City, 1894; member of the American Medical Association; died June 14, aged 77.

Crescenzi, Thomas Louis, Katonah, N. Y.; University and Bellevue Hospital Medical College, New York, 1927; member of the American Medical Association; attending physician at Lincoln Agricultural School in Lincolndale; physician for the public schools in Katonah and St. Mary's Parochial School; affiliated with Northern Westchester Hospital in Mount Kisco, where he died April 30, aged 48.

Crimmin, Leo Philip, Brockton, Mass.; Tufts College Medical School, Boston, 1917; served during World Wars I and II; died June 18, aged 54, of tuberculosis.

Dickie, Herbert Grasty, Roseland, Va.; University of Virginia Department of Medicine, Charlottesville, 1907; died May 7, aged 66.

Dwyer, William ✠ Hartford, Conn.; Johns Hopkins University School of Medicine, Baltimore, 1913; on the staff of Hartford Hospital; died June 24, aged 63, of cirrhosis of the liver.

Hanna, Benjamin M., East Orange, N. J.; Jefferson Medical College of Philadelphia, 1877; died in East Orange General Hospital June 7, aged 91.

Hendershott, Roy Wheeler, Bend, Ore.; University of Oregon Medical School, Portland, 1917; for many years physician for the Bend High School football team; affiliated with St. Charles Hospital; died May 31, aged 73, of heart disease.

Hilling, James Riley, Covington, Ohio; Hospital College of Medicine, Louisville, 1905; served on the staffs of Mercy and Portsmouth General Hospital in Portsmouth and Middletown (Ohio) Hospital; died June 18, aged 71, of heart disease.

Kell, Thomas Banks ✠ Fort Lawn, S. C.; Medical College of South Carolina, Charleston, 1900; died in Rock Hill May 31, aged 77.

McCune, Scott Scowcroft ✠ Santa Monica, Calif.; Harvard Medical School, Boston, 1932; specialist certified by the American Board of Internal Medicine; served during World War II; formerly affiliated with the Hospital of the Good Samaritan in Los Angeles; died June 3, aged 46.

Newton, Philip, New York; Georgetown University School of Medicine, Washington, D. C., 1910; at the outbreak of World War I joined a Red Cross unit in Russia and later became a general in the Imperial Russian Army; died June 18, aged 66.

Norton, James M., Arkadelphia, Ark.; College of Physicians and Surgeons, Little Rock, 1911; member of the American Medical Association; died June 16, aged 64.

Parodi, Teofilo, New York; Regia Universitá degli Studi di Genova Facoltá di Medicina e Chirurgia, Italy, 1888; member of the American Medical Association and the New York Academy of Medicine; at one time director of the Italian Hospital; died May 4, aged 84, of arteriosclerotic heart disease.

Phipps, Isom H., Mount Vernon, Ill.; Kentucky School of Medicine, Louisville, 1892; died May 31, aged 84.

Pyles, William Thomas, Eagle Rock, Va.; Medical College of Virginia, Richmond, 1935; died in Chesapeake and Ohio Hospital in Clifton Forge, April 28, aged 46, of heart disease.

Schenck, George Frederick, Los Angeles; College of Physicians and Surgeons, Los Angeles, 1917; associate professor of urology at the College of Medical Evangelists; member of the American Urological Association; fellow of the American College of Surgeons; affiliated with Los Angeles County Hospital, Presbyterian Hospital-Olmsted Memorial, Cedars of Lebanon and California hospitals; served overseas during World War I; died June 5, aged 59.

Shufelt, Alson Anderson ✠ San Jose, Calif.; University of California Medical School, San Francisco, 1917; specialist certified by the American Board of Obstetrics and Gynecology; served during World War I; affiliated with O'Conner Hospital and Santa Clara County Hospital; died June 11, aged 58.

Underwood, John B., St. James, Mo.; Barnes Medical College, St. Louis, 1901; member of the American Medical Association; died June 18, aged 84, of a cerebrovascular accident and arteriosclerosis.

Van Altena, Louis A., Cedar Grove, Wis.; Milwaukee Medical College, 1895; member of the American Medical Association; served as health officer; affiliated with Memorial Hospital in Sheboygan; died in St. Nicholas Hospital in Sheboygan, June 7, aged 80, of coronary thrombosis.

Van Duzer, William Roy ✠ Casey, Iowa; Jefferson Medical College of Philadelphia, 1912; served as a member of the town council, school director and local health officer; surgeon for the Rock Island Railroad; affiliated with the Atlantic Memorial Hospital in Atlantic, where he died June 20, aged 65, of myocardial infarction.

Van Noy, Levi Tipton, Norwood, Mo.; Ensworth Medical College, St. Joseph, Mo., 1904; member of the American Medical Association; died May 19, aged 74, of coronary disease and cerebral hemorrhage.

Walker, Madison Frank, Santa Fe, Tenn.; University of Tennessee Medical Department, Nashville, 1890; died May 30, aged 89, of coronary occlusion.

Ward, Thomas Eugene ✠ Houston, Texas; College of Medical Evangelists, Los Angeles, 1930; served as medical superintendent of the Wabash Valley Sanitarium in Lafayette, Ind.; died recently, aged 53, of coronary occlusion.

Watkins, Charles Napoleon, Fort Recovery, Ohio; Ohio Medical University, Columbus, 1904; served during World War I; died in Jay County Hospital, Portland, Ind., June 19, aged 73.

Whiddon, Rufus C., ✠ Gainesville, Texas; Baylor University College of Medicine, Dallas, 1910; fellow of the American College of Surgeons; past president of the Cooke County Medical Society; city physician; local surgeon for the Missouri, Kansas and Texas Railway; affiliated with Medical and Surgical Hospital and Gainesville Sanitarium; physician for State School for Girls; died June 19, aged 63, of coronary occlusion.

Williams, Lowell Eugene, Seattle; University of Minnesota Medical School, Minneapolis, 1927; member of the American Medical Association; served during World War I; on the staff of Virginia Mason Hospital; died June 3, aged 55, of coronary sclerosis and occlusion.

Young, L. Otis, Dawson Springs, Ky.; Southwestern Homeopathic Medical College and Hospital, Louisville, 1897; died June 13, aged 78, of cerebrovascular accident.

FOREIGN LETTERS

ITALY

(From a Regular Correspondent)

NAPLES, June 30, 1950.

Reports by Drs. D. Gottlieb and Perrin H. Long (U.S.A.) at the Second Italian Congress on Antibiotics

An important congress on atibiotics was held in Milan the first week of June; many foreign scholars participated, and Sir Alexander Fleming acted as chairman. The congress was organized by Prof. E. Carlinfanti, director of the Information Center for Studies on Antibiotics and the Italian Serotherapeutic Institute.

Reports were presented by Drs. Fleming, M. Curtin, A. D. M. Douglas, A. H. El Ramli, D. Gottlieb, R. Green, Perrin H. Long, P. Lopez Cardone, K. Pietz, R. Reitler, V. Ristich, O. Ruziczka and T. Schönfelder. Italian scientists were represented by the rector of the University of Milan, Professor De Francesco, by the dean of the faculty, Professor Cazzaniga, and by many authorities from the Italian medical and surgical world, among them the oncologist Bucalossi, the phthisiologists Carpi and De Sanctis Monaldi, the surgeon Fasiani and the bacteriologist Professor Zironi.

Fleming stated that he prefers the watery suspensions of procaine penicillin among the new types of commercial penicillin preparations and that only in more urgent cases does he consider it advisable to combine it with a small dose of sodium penicillin, which becomes adsorbed immediately. He discussed chloramphenicol, aureomycin and terramycin. He confirmed that the indications for all three overlap. These substances exert their action on pyogenic cocci, gram-negative bacilli of the colityphoid group, Brucella, the rickettsiae and on some virus types. However, the majority of the viruses has not yet been attacked by the antibiotics. According to Fleming, the three new antibiotics are highly active with respect to the majority of the intestinal micro-organisms, as within twenty-four hours of their administration cultures made from feces may contain only some mycetes and some ferments. This might be an advantage in abdominal surgical intervention, although according to Fleming this may deprive the patient of the vitamins elaborated by the intestinal bacteria. He therefore suggests concurrent administration of adequate vitamins.

Dr. D. Gottlieb reported on his observations of a Streptomyces isolated from the soil. Chloramphenicol was obtained and later synthesized. In the synthesis of this antibiotic many isomers may appear, owing to the position of the nitro-group and to the presence of two asymmetric atoms of carbon. Only one of these isomers is active, but its separation is not easy. Many derivatives of chloramphenicol have been prepared, but the only one which possesses activity (but only 14 per cent of the activity of chloramphenicol) is the nitroacetyl derivative. Chloramphenicol inhibits the activity of the esterases of bacterial origin in addition to some lipases, and some bacterial enzymes determine the hydrolysis of chloramphenicol. Administered by mouth, this drug is rapidly adsorbed from the gastrointestinal tract. Its products of transformation accumulate in the tissues within a short time and then are eliminated: in man, mainly through the kidneys; in animals, through the feces.

Aureomycin and Chloramphenicol

Dr. P. H. Long discussed the pharmacology and toxicology of all the antibiotics. The most detailed part of his report dealt with chloramphenicol and aureomycin. He emphasized the usefulness of their combined employment in endocarditis due to gram-negative bacteria. The effective level of orally administered chloramphenicol is obtained within eight hours after administration. Presumably the drug passes into the circulating blood and the intercellular fluids; otherwise there would be no explanation for its action in rickettsiosis. The speaker studied and reported on the antibiotic in the cerebrospinal fluid, in the pleural fluid, in the bile and in the milk. The drug also passes through the placenta, and from that results its prophylactic usefulness in the prenatal period. He believes that the dose of any antibiotic can be reduced to 50 per cent forty-eight hours after defervescence and discontinued five to seven days after that.

Syphilis and Antibiotics

A report on this subject was presented by M. Monacelli, director of the institute of dermatology and syphilology of the University of Naples. He stated that the antisyphilitic action of penicillin is proved but the therapeutic scheme may still be improved. It seems advisable to combine the antibiotic with other antisyphilitics. Monacelli discussed the absence of a relation—within certain limits—between the doses employed and the therapeutic effects, the value of a penicillin course in neurosyphilis and the eventual effect of penicillin on latent syphilis. He reported on research studies carried out in cooperation with Professor Tesauro, the director of the obstetric clinic of the University of Naples, concerning the penicillin treatment of pregnant women with syphilis.

Streptomycin Resistance

Professors G. Daddi and C. Panà reported on streptomycin resistance. They revealed that, in spite of the presence of streptomycin-resistant strains of tuberculosis bacilli, the administration of streptomycin continues to be efficacious. Reports concerning efficacy of the drug and resistance to it showed a discrepancy between results in man and those in animals. In man streptomycin resistance is not associated with characteristic deterioration as it is observed in animals when administration of the drug is continued in spite of the observed resistance.

The congress was adjourned after four days of intensive work and many reports. Professor Carlinfanti as the organizer of the congress, in cooperation with Dr. Gianferrari, received considerable praise from Professor Fleming.

Prof. Hans Selye from Montreal in Bologna

While the congress on antibiotics was held in Milan another meeting took place in Salsomaggiore on the occasion of the international medical and surgical motion picture fair. It was obvious that the motion pictures from the United States met with greatest success. The pictures were furnished by the United States Information Service (U.S.I.S.). Many Italian clinicians participated in this convention, with Prof. Maurizio Ascoli, who at 74 years of age still holds the chair of the University of Palermo, as their chief. The congress of Salsomaggiore was organized by the S.A.G.A.S. to emphasize the value of the well known sodium iodine spas in this region.

In Bologna, close to Salsomaggiore, Prof. Hans Selye held a conference as the guest of Prof. A. Gasbarrini, director of the university institute of the medical clinic. As a symbol Selye presented to Gasbarrini the first copy of his book "Stress," stating that in this clinic, which was one of the first in Italy, the first concrete observations were made on the influence of the adrenal cortex and the general states of reaction. These observations contributed largely to the development of the concept of "syndromes of adaptation."

SWEDEN

(From a Regular Correspondent)

STOCKHOLM, July 14, 1950.

Erythema Nodosum as a Guide to Tuberculosis Morbidity

Recent Scandinavian studies have shown that in earlier years most cases of erythema nodosum, particularly juvenile cases, are indicative of infection with tubercle bacilli. At present it seems that, in Sweden at any rate, more than half the cases of erythema nodosum treated in hospital are nontuberculous and are due to streptococcic and other infections. Dr. Sven Löfgren, of the Tuberculosis Department of St. Göran's Hospital in Stockholm, has published in the organ of the Swedish Medical Association for June 2, 1950 an investigation indicative, in his opinion, of a pronounced decline in the tuberculosis morbidity rate.

The evidence with which Dr. Löfgren supports his thesis is partly statistical, partly clinical and bacteriologic. The statistical evidence deals with the years 1942 to 1949 (with the exception of 1945, for which data were not available). During this period the reports of cases of erythema nodosum to the central dispensary in Stockholm showed a definite decline. In the first three years of this period (1942 to 1944) there was an average every year of 233.7 cases of erythema nodosum in female patients. The corresponding figure was down to 185.0 in the next period (1946 and 1947), and in the last two years (1948 and 1949) the annual average was only 116.5. The corresponding figures for cases in male patients were 46.0, 36.5 and 20.5. In the same period there was a significant decline in the number of cases reported in the younger age groups in which tuberculosis is most frequently the cause of erythema nodosum. In the older age groups, streptococcic infections and sarcoid lesions were the predominant factors responsible for erythema nodosum.

Turning to the clinical evidence, Dr. Löfgren points out that in the most recent years the patients with eyrthema nodosum admitted to St. Göran's Hospital have mainly had the nontuberculous type. Indeed, during 1949, when 31 patients with erythema nodosum were admitted to this hospital, only 3 of them had the tuberculous type. A little earlier in the same hospital 10 of 58 cases were of the tuberculous type. The conclusion drawn from all this evidence is that erythema nodosum of the tuberculous type has declined in frequency because of change in conditions conducive to infection with virulent tubercle bacilli. Credit for this is given in some quarters to the antituberculosis campaign with its BCG vaccination, to the discovery of infectious cases of tuberculosis by mass radiography and to modern chemotherapy.

The Shortage of Doctors and Nurses

The decision to reduce the number of Austrian doctors to be imported into Sweden from about 200 to 100 reflects the many objections to this scheme from various quarters. The present shortage of doctors was dealt with recently in a debate in the Swedish Parliament. Several attempts were made on this occasion to learn the causes of the present shortage of doctors, and one speaker referred to the rather fanciful calculation that the work of filling in forms and other clerical duties were equivalent to the full time working capacity of 600 doctors (in 1947 the total number of doctors in Sweden was 4,234). Such a calculation is a gesture of protest against clerical work which should be passed on to laymen.

One speaker said that as many as 173 hospital departments have been closed for want of nursing and subordinate staff members; in 143 of the 173 the closure was due to lack of nurses. A sanatorium department had been closed for four months for want of doctors, and this was not an isolated case. With the help of the many foreign doctors already in Sweden and coming to the country in the near future, and with the output in a few years' time of young Swedish doctors from the new High School of Medicine in Gothenburg, this state of affairs should be remedied. Meanwhile the impression was gained from the debate that many laymen in Sweden are critical of the attitude of the Swedish Medical Association toward these problems and toward Dr. Axel Höjer, who as head of the Public Health Service is reported to have found himself in conflict with a large section of the medical profession.

Addition of Vitamin D to Milk

The discussion on March 3 at a meeting of the Swedish Medical Society threw much interesting light on the conditions under which milk is sold in Stockholm. Ever since 1937 the addition of vitamins to milk has been under discussion. One variety of milk on the market in Stockholm costs an additional 2 öre per liter because vitamin D has been added to it. The milk in question contains about 450 international units of this vitamin per liter. During the bargaining which preceded the fixing of this higher price, the milk vendors asked for 5 öre, though the actual cost of the added vitamin was only 0.018 öre per liter. It was calculated that, in terms of Swedish öre, a Swede pays 40 per liter for milk, while an Englishman pays 53 and an American pays 87.

BELGIUM

(From a Regular Correspondent)

July 10, 1950.

International Congress of Gerontology

The first International Congress of Gerontology was held in Liège under the presidency of Professor Brull. Numerous internationally known authorities participated because the foundation of the International Association of Gerontology was to be discussed at this Congress. Many communications were presented on diseases of the heart, the kidneys and the blood vessels and on numerous social questions and problems of nutrition.

Dr. Nizet of Liège discussed blood disorders of the aged, and Professor Brull reported on the organization of data on the influence of nutrition on senescence and on resistance to tuberculosis. Drs. Morpurgo and Beselli spoke of protein changes in the aged and of research work on the reactions of colloidal lability and of electrophoresis. Professor Turnbridge reported studies on the nature of cutaneous modifications in the aged. Professor Jacques Roskam, professor at the University of Liége, spoke on euthanasia. He reported a case of pure vegetative survival in cerebral sclerosis, and he considered the problem of euthanasia, dysthanasia and orthothanasia. He formally condemns euthanasia. However, on the occasion of a particularly striking observation and considering the increasing number of long, artificial survivals, strictly vegetative, he asks whether omission of certain procedures in such hopeless and definite cases would not be morally, socially, and humanely a solution to this new problem. The question would lose its importance if gerontologic technics could prevent senescence, or if the hospital capacity and the supply of nurses in the various countries were considerably increased. After an animated discussion it became apparent that this problem must be studied carefully in an entirely impartial manner. Professor Roskam has considered these ideas in investigations at the School of Criminology of the Faculty of Laws of the University of Liège and at the Medico-Juridico Committee of Monaco, at which papers have been presented on related subjects and especially on various questions regarding an international medical law.

CORRESPONDENCE

HEALTH INSURANCE PLAN OF GREATER NEW YORK

To the Editor:—After reading Dr. George Baehr's description of the Health Insurance Plan of Greater New York, as published in THE JOURNAL (**143**:637, June 17, 1950), one would think that the subscribers and physicians concerned had arrived in Medical Utopia. The estimable reputation of the author is sufficient assurance of his sincerity. However, it should be pointed out that some of the statements made were either incomplete or inaccurate.

The benefits accruing to both patients and physicians from group practice as opposed to individual practice cannot be disputed. Because of this I became senior internist in a component group of the Health Insurance Plan when it began operations early in 1947. At the end of eighteen months neither I nor nearly one half of the group's physicians accepted the Health Insurance Plan's request to renew their contracts, which expired at that time.

In relating the history of the organization Dr. Baehr omitted to mention that its first sponsor was his late patient the Honorable F. H. LaGuardia, then Mayor of the City of New York. When the county societies raised certain objections to the proposed plan, the mayor countered with the threat to "import" doctors if sufficient numbers of physicians practicing in New York City refused to participate. Furthermore, the plan was launched at a time when many physicians recently returned from military service looked at the prospect of reestablishment with pessimism. In spite of its imperfections the Health Insurance Plan promised them a living wage without delay. The enabling law, enacted by the New York State Legislature for the benefit of the plan, legalized partnership practice in this state. In a partnership each individual is responsible for not only his own professional conduct but also that of each of the other partners. The city government headed by the mayor agreed to pay one-half the premium for each employee enrolled. However, similar consideration is not given to employees who prefer some other form of health insurance such as that offered by the Blue Shield Plan. Thus Dr. Baehr's claim that enrolment in the Health Insurance Plan is entirely voluntary and not discriminatory should have been qualified.

Dr. Baehr mentioned that 75 per cent of a group having a common employer was required before enrolment of the group could be accomplished. In the case of the city, the common employer was interpreted to mean head of a department or unit with 25 or more employees. In industry and business, the head of a union local was loosely termed the employer.

The provision for exclusion of those earning over $5,000 emanated from representatives of the county medical societies, whose endorsement the Health Insurance Plan found desirable. Dr. Baehr stated that because of this provision certain business and industrial groups refused to consider enrolment for their members. He did not state that the organization was and is in favor of no exclusion for the reason that workers in an organization are apt to follow the actions and suggestions of their foremen or supervisors. If the latter are eligible to join, the necessary quota is much easier to secure. Although the Health Insurance Plan repeatedly disavowed actual coercion, it openly encouraged "eager persuasion."

The contract between the Health Insurance Plan and the medical groups makes the partners individually and collectively responsible to the organization. The group must not only insure itself against every form of litigation but must also insure the Health Insurance Plan, which guarantees nothing to the group except payment of the capitation fee for each patient desiring enrolment in the group. The number of patients is not guaranteed, although the contract if fully enforced requires the investment of considerable money by the partners in a building whose physical details must be approved by the plan. The equipment, technicians and other employees are dictated by the plan. The published average net income of physicians up to now does not take into account these provisions, which up to the present have been waived orally because the enlistment of adequate numbers of physicians to man the plan would have been discouraged. The answer to what happens if, after all demands have been met, the Health Insurance Plan terminates or refuses to renew its authorization to treat its enrolled subscribers or decides to reduce the quota of patients allotted to each group, has as yet not been given. With twenty of twenty-eight group centers still in the planning stage, Dr. Baehr was most vague as to whether the $10,000 average net income was what it now is, or whether this is the figure anticipated when each group has a full quota of 20,000 patients and is maintaining and operating a group center. The Health Insurance Plan has never expressed its intention to limit the ratio of patients to groups in the order of 20,000 to 1. In short, the group must acquire valuable assets not easily liquidated, while the organization can give no assurance of fixed income, fictitious or actual.

Dr. Baehr says "The groups are comprised of physicians and specialists who represent a good cross section of the reputable members of the medical profession of the city." The criteria used to arrive at this conclusion were not mentioned. Physicians who are advocates of the plan as well as those who participate in the treatment of patients as members of one or more medical groups fall into certain categories. A handful is interested in group practice for its own sake and is noncommittal about the insurance aspect of the plan. Some, like Dr. Baehr, believe the plan to be an important bulwark against proposed national health insurance. Many of these, however, have not been interested in partnership in one or more medical groups. They have income from sources other than ordinary medical practice, or their private patients are of the type who would not be interested in the plan's service even if it were offered to them. Another group sees increased income and other opportunities available by joining the plan. Finally, another group joined the plan because they saw a large segment of their practices consisting of city employees and members of labor unions being taken into the fold. Perhaps the yardstick used was membership in a county medical society, which the Health Insurance Plan requires. This lip service is very practical for the organization, inasmuch as malpractice insurance which will protect partners collectively as well as individually is issued only to those subject to censorship by virtue of their membership in a county medical society. Furthermore, appointment to the staffs of most voluntary and proprietary hospitals depends on the same requirement.

The author mentioned participation on the Medical Control Board of representatives of "two of the larger county medical societies." Five societies are concerned. The latest available data indicate that the majority of physicians belong to the other three (Bronx, Queens and Richmond). None of the five medical societies actually approves of the Health Insurance Plan, because it does not choose to conform to the principles for voluntary health insurance plans and group practice enunciated by the American Medical Association and the state medical society. The three medical groups without representation felt that they could not create a paradox by accepting the plan's repeated invitations to send representatives.

The autonomy of each group center is emphasized. Except as stated, the plan has no concern with the group's internal affairs so long as there is no evidence of dissatisfaction from patients. From the results of the survey which Dr. Baehr describes it is apparent that the democratic principle of group sovereignty cannot always be strictly followed. Most certainly the Health Insurance Plan must see to it that a group's performance at least equals the record of individual practice. Furthermore, the organization supposedly opposes exploitation of one or more physicians in a group by a majority of their fellows. The contention that resignation will automatically follow dissatisfaction is untenable, for reasons to be discussed herein.

Most physicians recognize how little value there is in a layman's appraisal of good medical care. His silence is certainly a poor gage of efficiency. Many physicians have patients on the rolls of the Health Insurance Plan though they use the service infrequently or not at all. The clinical records in the files of a group do not necessarily reveal the facts obtained by a nonplan physician to whom the patient may turn. As Dr. Baehr intimated, the survey was made for the purpose of self correction. However, it is strange that not one of the physicians who have since terminated their connection with the Health Insurance Plan has ever been subsequently interviewed by the surveyors. Not even the mass exodus of nearly half a group was considered a symptom of any significance.

It should be natural to ask why not more than perhaps 5 per cent of physicians have not been disgruntled enough to sever their relationship with the Health Insurance Plan. As previously pointed out, resignation from a partnership or termination of the contract with the plan without the consent of the partners and the organization does not exclude the individual from financial responsibility until the period of time specified has elapsed. The first contract of the Health Insurance Plan expired after eighteen months. Subsequent contracts are for longer periods. It may also be asked why there is a waiting list of groups to be activated, if there is any considerable dissatisfaction. Some of the circumstances attending the inauguration of the plan have been related. The policies were sold by commissioned salesmen with the aid of profusely illustrated brochures and newspaper advertising with dramatic appeal. Despite the stated refusal of physicians to have their names used for advertising purposes, printed lists of physicians in the Health Insurance Plan were shown to prospects. Were it not for certain hampering influences exerted by many members of the medical profession who were called "reactionary," "shortsighted" and "selfish," enrolment would have increased more rapidly than it has.

None the less, many physicians faced the loss of a major number of their patients and heeded the warning to join a group "before it is too late"—in other words, before the doors were closed. The Health Insurance Plan with subscriber contracts already in force actually pressed the groups to complete their organization and get started, with the warning that latecomers might not be served.

It requires a major adjustment of one's philosophy to relinquish a certainty in exchange for a possibility. This difficulty is increased when fixed expenses such as taxation and support of a family go on implacably. Many specialists now or formerly affiliated with the Health Insurance Plan automatically burned their bridges behind them. Naturally former sources of referral with which the groups competed dried up. The possibility of reconciliation on resignation was too much of a gamble for most. Since the organization now has available more professional personnel than it needs, it is in a position to reduce the cost of policies for one reason or another and to offer less remuneration to medical groups without materially endangering its ability to supply subscribers with medical service. It cannot be overemphasized that the only obligation which the Health Insurance Plan assumes is to furnish the subscriber with the name of a group operating in or near his community. Dr. Baehr's glowing report to the contrary, it should be remembered that "all is not gold that glittters."

ELMER A. KLEEFIELD, M.D., Forest Hills, N. Y.

CANCER AND TOBACCO SMOKING

To the Editor:—Two articles published in the May 27 issue of THE JOURNAL "Tobacco Smoking and Bronchogenic Carcinoma," by Ernest L. Wynder and Evarts A. Graham, and "Cancer and Tobacco Smoking" by Morton L. Levin, Hyman Goldstein and Paul R. Gerhardt, represent the past and present clinical approach to the cancer problem but completely miss some of the extremely interesting and basic aspects of the disease. Both articles fail to emphasize the elemental cellular unit, which is the heart of the entire problem. No matter how early cancer is seen clinically, it is biologically late, and the entire philosophy of investigation must move to this level if we ever hope to effect a cure. To illustrate from the two papers noted, in tobacco tar a benzpyrene compound can be readily isolated and, when applied to normal cells, can alter the genetic structure so that a cancer cell can be produced according to well established genetic laws. A most valuable contribution to this entire problem was omitted, namely, in both papers a carcinogenic compound (benzpyrene) may also act as a mutagenic compound. To put the same principle more tritely, the clinical investigation cannot advance to profoundly effect a cure until the clinician appreciates some simple principles of genetics which can be easily and readily obtained.

EDWIN J. GRACE, M.D., Brooklyn.

CHEMICAL STRUCTURE AND SENSITIVITY

To the Editor:—I have read with extreme interest the case report of Dr. David G. Welton which appeared in THE JOURNAL May 20, 1950, on "Exfoliative Dermatitis and Hepatitis Due to Phenobarbital."

I am writing to inform you of an article entitled "Dilantin Sensitivity, Report of a Case of Hepatitis and Jaundice, with Pyrexia and Exfoliative Dermatitis," by Goldberg, Segal and me which will appear in the *New England Journal of Medicine* June 8, 1950. Our case is remarkably similar to Dr. Welton's with respect to exfoliative dermatitis, pyrexia, eosinophilia, hepatitis and jaundice, which we attributed to dilantin® (diphenylhydantoin sodium), which the patient had started to take three weeks prior to onset. Resumption of treatment with the drug inadvertently caused an exacerbation of symptoms in our case.

Another interesting report linking the effects of these drugs, diphenylhydantoin sodium and phenobarbital, which are chemically similar, and that of nirvanol® (phenylethylhydantoin), another member of this group, was that by Ellis, "Reactions to Nirvanol, Phenytoin Sodium (Dilantin) and Phenobarbital, Report of a Case of Ectodermosis Erosina Pluriorificialis After Phenytoin Sodium" (*South. M. J.* **36**:565 [Aug.] 1943). It is interesting, therefore, to observe how drugs related structurally can elicit similar sensitivity manifestations as well as pharmacologic effects.

In view of the widespread use of these drugs, a greater awareness on the part of physicians of the possible widespread and systemic reactions that these drugs can elicit is important. In this era of increased awareness of the importance of anaphylaxis in disease and the use of ACTH in such reactions these reports assume more importance.

BERNARD H. CHAIKEN, M.D., Boston.

CURRENT MEDICAL LITERATURE

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

79:785-972 (May) 1950

Clinical Observations on New Sulfonamide (Gantrisin®). J. A. Bigler and O. Thomas.—p. 785.
Approach to Psychiatric Problems in Childhood. M. Kaplan.—p. 791.
Simultaneous Nonfatal Systemic Histoplasmosis in 2 Cousins. W. E. Wheeler, V. Friedman and S. Sasiaw.—p. 806.
Thrombopenic Purpura: Report of 4 Cases in One Family. M. H. Roberts and M. H. Smith.—p. 820.
Urinary Excretion of Glucuronic and Salicylic Acids in Normal and in Rheumatic Children. J. C. S. Tseng, H. W. Elghammer and A. C. Ivy.—p. 826.
Paroxysmal Supraventricular Tachycardia in Infancy: Review of Treatment and Report on Infant Treated with Methacholine (Mecholyl®) Chloride. W. M. Brownlee, E. M. Waters and S. J. McClendon.—p. 838.
Bronchial Changes in Experimentally Induced Cystic Degeneration of Pancreas. P. V. Véghelyi, T. T. Kemény and J. Sós.—p. 846.

American Journal of Medical Sciences, Philadelphia

219:473-588 (May) 1950

Arterial Insufficiency Studied by Several Plethysmographic Techniques Employing Occlusion of Arteries of Extremity. T. Winsor, R. E. Morrison, B. O. Kondo and P. Yamauchi.—p. 473.
Treatment of Peripheral Neuropathy in Diabetes Mellitus. W. S. Collens, A. M. Rabiner, J. D. Zilinsky and others.—p. 482.
Study of Renal Function in Patients with Multiple Myeloma. J. B. Armstrong.—p. 488.
Use of Phenylacetylurea (Phenurone) in Convulsive Disorders. S. C. Little and R. R. McBryde.—p. 494.
Abnormal Electrokymograms from Wall of Ventricle With and Without Evidence of Myocardial Infarction. F. G. Gillick and J. Schneider.—p. 500.
Rupture of Heart Following Myocardial Infarction: Data from Small Hospital. A. H. Clagett Jr., J. H. Benge and J. W. Hooker.—p. 513.
New Test for Vasopressor Substances in Hypertension. D. B. Fishback.—p. 517.
*Coincidence in Autopsy Material of Nephrosclerosis and Cardiac Hypertrophy with Clinical History of Hypertension. J. L. Switzer and F. Osterman.—p. 523.
*Thrombocytopenic Purpura: Prognostic and Therapeutic Value of Eosinophil Index, Analysis of 100 Cases. S. O. Schwartz and S. R. Kaplan.—p. 528.
Blood "Sludge" Phenomenon in Human Subjects: Notes on Its Significance and on Effects of Vasomotor Drugs. H. S. Robertson, S. Wolf and H. G. Wolff.—p. 534.
Clinical Evaluation of Blood "Sludge" Phenomenon. J. S. Hirschboeck and M. Woo.—p. 538.
Electrocardiographic Patterns in Hypopotassemia: Observations on 79 Patients. S. Bellet, W. A. Steiger, C. S. Nadler and P. C. Gazes.—p. 542.
Cerebral Angiography. J. F. Roach.—p. 559.
Aureomycin. W. E. Herrell.—p. 570.

Nephrosclerosis and Cardiac Hypertrophy.—Switzer and Osterman studied the necropsy protocols of 4,168 patients of Cook County Hospital, Chicago, in which at least one of the three factors, cardiac hypertrophy, arteriolar nephrosclerosis and hypertension before death was recorded. Coincidence of all three factors was found in 21.7 per cent of the cases with heart weight above 500 Gm. and in 32.6 per cent of the cases with a heart weight greater than 350 Gm. Only part of this relatively low incidence of simultaneous occurrence of these three factors can be explained by a terminal drop in the blood pressure secondary to cardiac failure or peripheral vascular collapse. Death from congestive heart failure was observed in two-thirds of the cases in which cardiac hypertrophy and nephrosclerosis were found without elevation of the blood pressure above 150/90. Increased weight of the heart in the absence of either nephrosclerosis or recorded hypertension was observed in a significant number of, i. e., in 5 per cent of the cases with heart weight above 500 Gm. and in 18 per cent of the cases with heart weight greater than 350 Gm. Cardiac hypertrophy may be observed at necropsy in the absence of hypertension, nephrosclerosis, valvular, myocarditic or pulmonary lesions and congenital anomalies. The coexistence of cardiac hypertrophy, hypertension and arteriolar nephrosclerosis is the exception rather than the rule.

Thrombocytopenic Purpura.—Schwartz and Kaplan report on 100 patients with primary thrombocytopenic purpura. Previous observations suggested the existence of a significant correlation between the number of eosinophils in the marrow and the clinical course. The term eosinophile index related to the numbers of eosinophils observed in the marrow. The patients were divided into 2 groups, those with a high eosinophil index and those with a low eosinophil index. Significant prognostic differences were noted between the two groups. Fifty-four (83 per cent) of 65 patients with a high eosinophil index were cured (29 of them spontaneously), and, more significant prognostically, none of the splenectomized patients died. Sixteen (46 per cent) of 35 patients with a low eosinophil index were cured (8 of them spontaneously) while 8 (44 per cent) of the splenectomized patients died despite surgical therapy. The total number of deaths before splenectomy was 13; 6 of these occurred in the high eosinophil index group (9 per cent) and 7 in the low index group (20 per cent). Thus patients with a high eosinophil index showed a marked tendency for spontaneous recovery, practically certain cure by splenectomy and insignificant operative mortality. Patients with a low eosinophil index showed a slight tendency for spontaneous recovery, splenectomy was therapeutically unreliable and both the operative and over-all mortality were high.

American Journal of Medicine, New York

8:559-688 (May) 1950

SYMPOSIUM ON VIRAL HEPATITIS

Note on History of Epidemic Viral Hepatitis in Germany. H. T. Gardner.—p. 561.
Endemiologic Aspects of Hepatitis in U. S. Troops in Germany 1946-1950. J. R. Paul and H. T. Gerdner.—p. 565.
Evaluation of Two Screening Tests for Detection of Early and Subicteric Viral Hepatitis. W. E. Swift Jr., W. N. Miller, F. H. Streitfeld and M. Knowlton.—p. 581.
Serum Cholesterol and Cholesterol Esters in Viral Hepatitis. H. T. Gardner, W. E. Swift Jr., M. Modica and others.—p. 584.
Factors Influencing Retention of Bromsulfalein in Blood of Patients with Viral Hepatitis. W. P. Havens Jr., W. N. Miller, W. E. Swift Jr. and others.—p. 591.
Comparison of Thymol, Cephalin-Cholesterol Flocculation and Colloidal Red Tests in Acute Viral Hepatitis. J. R. Neefe, J. M. Gambescia, H. T. Gardner and M. Knowlton.—p. 600.
Oral Cholecystography in Patients with Viral Hepatitis. H. M. Readinger, W. E. Swift Jr., H. T. Gardner and J. A. Sheedy.—p. 611.
Clinical Course of Viral Hepatitis and Effect of Exercise During Convalescence. W. E. Swift Jr., H. T. Gardner, D. J. Moore and others.—p. 614.
*Myocardial Infarction Without Anticoagulant Therapy: Deaths Emboli and Analysis of Factors Influencing Mortality. N. Doscher and C. A. Poindexter.—p. 623.
Effects of Orally Administered Dihydroergocornine (D.H.O. 180) on Hypertension. C. T. Bello, W. G. Moss and E. Weiss.—p. 634.
*Digitalis Poisoning. W. B. Burwell and J. P. Hendrix.—p. 640.

Myocardial Infarction Without Anticoagulant Therapy.—Doscher and Poindexter present an analysis of 414 consecutive cases of myocardial infarction not treated with anticoagulants. Their observations suggest that the possibility of death from myocardial infarction is materially affected by sex, age

and the presence or absence of previous infarction. In the evaluation of therapeutic procedures both treated and untreated patients must be classified as to sex, age groups and previous status in order that an unbiased comparison may be made. The use of average ages is misleading since significantly different age distribution curves may give identical figures for average age. The mortality rate from myocardial infarction is about 50 per cent higher in women than in men. It follows that sex distribution will influence the mortality rate. Hypertension has an adverse effect on the outcome. Angina and other evidence of cardiac embarrassment have an unfavorable influence on the mortality rate. Major thromboembolic phenomena unfavorably influence the recovery of the patient. However, the authors found that thromboembolic phenomena have little effect on the mortality rate. In only 1 case could death be directly ascribed to thromboembolism. The authors do not wish to be critical of dicumarol® or of any other type of therapy in myocardial infarction. Anticoagulant therapy may be a distinct advance in the treatment of coronary thrombosis or even coronary sclerosis. However, the state of the heart at the time of infarction must be weighed in the statistical analysis of the effectiveness of any therapeutic procedure.

Digitalis Poisoning.—Burwell and Hendrix state that ambulatory patients have a fairly wide margin between therapeutic and toxic doses of digitalis, whereas this margin may be narrow in severe cases of heart disease. The rate of excretion of digitalis will vary with the amount in the body. The administration of mercurial diuretics to patients with congestive failure who have received considerable digitalis may be followed by rapidly increasing digitalis effects or intoxication, perhaps due to the mobilization of digitalis-containing fluid from the tissues and serous cavities. Requirements of the same patient for the drug change as the disease progresses or regresses. Digitalis is retained as successive doses are given; this cumulative action may lead to poisoning. Digitalis should be given by the oral route, because this seldom results in fatalities. Overdigitalization results easily when the drug is given by the intravenous route. The optimum dose of digitalis should not be defined as the dose which falls just short of toxicity but rather as the minimum dose required to produce the desired effect. This must be determined individually. The relief of congestive failure is the most reliable indication that effective doses are being employed. Abatement of a rapid ventricular rate, especially when associated with auricular fibrillation, is another valuable sign that an effective dose has been reached. Certain patients with congestive failure can derive only limited benefit from digitalis because of extensive myocardial damage; forcing the drug to toxic effects cannot bring relief. Thus the degree of improvement with digitalis is of some prognostic value. Other measures such as activity restriction, sodium chloride elimination and treatment with mercurial diuretics often will assist in controlling congestive failure when the benefit from digitalis alone is limited.

American Journal of Pathology, Ann Arbor, Mich.

26:349-500 (May) 1950

Distinctive Vacuolar Nephropathy Associated with Intestinal Disease. J. P. Kulka, C. M. Pearson and S. L. Robbins.—p. 349.
Parenchymatous Lesions of Liver and Kidney of Mice Due to Pectin. G. W. Richter.—p. 379.
Effect of Restriction of Fluid Intake on Production of Nephrosis in Rabbits. W. B. Wartman, J. M. Tucker and R. B. Jennings.—p. 389.
Experimental Total Midzonal Hepatic Necrosis. B. Black-Schaffer, D. J. Johnson and W. G. Gobbel Jr.—p. 397.
Intra-Uterine Respiration-Like Movements in Relation to Development of Fetal Vascular System: Discussion of Intra-Uterine Physiology Based Upon Cases of Congenital Absence of Trachea, Abnormal Vascular Development and Other Anomalies. G. Milles and D. B. Dorsey.—p. 411.
Sarcoidosis of Spleen: Report of 4 Cases with Twenty-Three Year Follow-Up in 1 Case. S. Kay.—p. 427.
Plasma Cell Tumors of Upper Respiratory Tract: Clinico-Pathologic Study with Emphasis on Criteria for Histologic Diagnosis. A. J. Rawson, P. W. Eyler and R. C. Horn Jr.—p. 445.
Benign Lymphoma of Rectum. E. L. Heller and H. H. Lewis Jr.—p. 463.
Pleural Mesothelioma. W. N. Campbell.—p. 473.
Histochemical Studies on Tissue Enzymes: V. Difficulty in Enzyme Localization in Acid Range Due to Selective Affinity of Certain Tissues for Lead; Its Dependence on *p*H. W. Newman, E. A. Kabat and A. Wolf.—p. 489.

Am. Practitioner & Digest of Treatment, Philadelphia

1:449-560 (May) 1950

Multiple Myeloma. W. M. Fowler and J. D. Gordon.—p. 449.
*Cholesterol Metabolism in Health and Disease: Its Relationship to Arteriosclerosis. L. N. Katz, J. Stamler and L. Horlick.—p. 461.
Rupture of Heart Muscle in Association with Myocardial Infarction: Some Points in Differential Diagnosis. J. M. Askey and C. B. Cherry.—p. 469.
Primary Malignancy of Liver. I. B. Brick.—p. 475.
Some Considerations in Differential Diagnosis of Chronic Diarrhea. W. T. Gibb Jr.—p. 480.
Some Psychosomatic Aspects of Respiratory Disease. A. Hurst, R. Henkin and G. J. Lustig.—p. 486.
BAL (2,3-Dimercaptopropanol) in Treatment of Arsenical Reactions. H. L. Holley.—p. 493.
Significance of Routine Urine Findings: Review of Urine Studies in 310 Consecutive Patients. G. A. Kriz.—p. 497.
Observations on Use of Intravenous Procaine as Antitumefaction Agent in Rhinoplastic Surgery. R. B. Lewy.—p. 500.
Periarticular Fibrositis in Coronary Disease. E. F. Traut.—p. 512.
Clinical Evaluation of Jacobson's Solution in Treatment of Chronic Pelvic Inflammatory Disease. M. Markowitz and C. W. Wick Jr.—p. 516.

Cholesterol Metabolism and Arteriosclerosis.—Katz and co-workers studied the relationship in chicks of cholesterol metabolism to arteriosclerosis. Chicks are naturally subject to spontaneous atherosclerosis of the great vessels. Hyperlipemia and experimental atheroma readily develop when chicks are fed cholesterol. The spontaneous and cholesterol-induced lesions resemble each other closely and are similar to human atherosclerosis. Experiments showed that minimal hypercholesterolemia and organ lipidosis occur with a low concentration of dietary cholesterol. Nevertheless preliminary observations indicated that atherosclerosis inevitably ensues in time. The lesion is apparently cholesterol induced and not spontaneous. In its origin it would appear to simulate closely human atherosclerosis, which often develops without frank hypercholesterolemia and organ lipidosis. Gross hypercholesterolemia and organ lipidosis occur as the concentration of cholesterol fed to the chick is increased. Atheroma appears earlier. By prolonged administration of lipid to the chick it is possible to reproduce experimentally the gamut of atherosclerotic lesions seen in man, except ulceration. The authors' studies failed to reveal any prophylactic effect of the lipotropic factors choline and inositol against spontaneous or experimentally induced atherosclerosis in young cockerels. In another experiment the authors followed the changes occurring when cholesterol feeding is stopped. Lesions moderate in extent and severity may "heal" and disappear. More severe atheroma may regress partially and undergo fibrosis, calcification and cartilaginous metaplasia. These observations confirm clinical impressions that atherogenesis in man is a discontinuous process and that atheroma may undergo regression and healing. The results of additional experiments did not negate the possibility that high cholesterol diets predispose to atheroma but afforded evidence against the idea that general restriction of cholesterol in the diet is insurance against atherosclerosis. Routine prohibition of foods rich in cholesterol would seem to have its chief indication in hypercholesterolemic states which may be amenable to dietary control. Desiccated thyroid proved of value against cholesterol-induced atherosclerosis in the chick but was ineffective in eliminating spontaneous atherosclerosis. It may even accelerate the onset of the spontaneous lesion. Experimental evidence does not warrant the clinical use of thyroid preparations for the treatment of arteriosclerosis. The concept that cholesterol is a key pathogenic factor in arteriosclerosis can hardly be denied today, but the precise pathways of cholesterol action remain to be charted.

Annals of Western Medicine & Surgery, Los Angeles

4:211-258 (May) 1950

*Paroxysmal Auricular Fibrillation in Association with Rheumatic Heart Disease: Study of Thirteen Cases. J. M. Askey and C. B. Cherry.—p. 217.
*Sludged Blood: Electrokinetic Factors Involved. C. J. Bellis and H. L. Snow.—p. 223.
Clinical Application of Unipolar Limb Leads. E. Phillips.—p. 227.
Relationship of Blood Iodine Level to Thyroid Function, with Report of Five Atypical Cases of Abnormal Thyroid Function. F. E. Harding and A. Vida.—p. 232.

Auricular Fibrillation with Rheumatic Heart Disease.—Askey and Cherry report 13 patients, 6 men and 7 women between the ages of 29 and 60, with rheumatic heart disease and paroxysmal auricular fibrillation. Either thromboembolism

or congestive failure or both occurred during a paroxysm in 9 of the 13 patients. To abort a paroxysm quinidine was given at the onset of an attack in doses of 3 grains every hour until the attack was terminated. The patient was first digitalized if the paroxysms became quite frequent and persisted longer. The daily administration of quinidine in doses of 3 grains, three times daily was tried, if digitalis proved ineffective. If this initial dose of quinidine was ineffective, it was increased to 6 grains three times daily. Attacks at night are probably due to lack of nocturnal quinidine effect. Enteric coated tablets at bedtime may be useful in providing nocturnal effect. Digitalis and quinidine were given in full dosage if either thromboembolism or congestive failure were concomitants of the attack. The paroxysms became markedly reduced in frequency in 11 of the 13 patients. Auricular fibrillations eventually became established in 4 of the 13 patients. In 3 of these, congestive failure became chronic and severe soon after the establishment of the arrythmia. Two of these patients died of congestive failure and multiple embolism within two years. The third is bedridden. The use of dicumarol at the time the arrythmia becomes established, dosage to be adjusted for continuous ambulant use, is advocated.

Sludged Blood.—Bellis and Snow observed sludged blood in 208 of 250 patients (83 per cent) whose conjunctival vessels were studied. About 20 patients (10 per cent) had extremely marked sludging. The majority of the patients had malignant tumors, diabetes mellitus or cardiovascular disease. The others had anemias, tuberculosis, alcoholism, mononucleosis, asthma, arthritis, nephritis, neurosis, rheumatic fever, hepatic cirrhosis, acute lymphadenitis and hyperparathyroidism. Eighty per cent of the patients were aged over 40. Changes in the plasma, such as variations in imbibed water, electrolyte concentration, and hydrion levels, are among the factors mediating the reduction in surface charge of the erythrocytes. The reduction of electrokinetic potential produces sludging (or agglutination) in order to reduce the free surface energy of the cells. Decrease of electrokinetic potential is necessary before hemocytes or bacteria can be phagocytosed. The virulence of bacteria is proportional to their electrokinetic potential. The phagocytosis of parasites by splenocytes and erythrocytes in malaria is due to adsorption by the cells which have undergone reduction in electrokinetic charge. Phagocytosis, whether in the inflammatory field or in reticuloendothelial organs, and marginations of cells in inflammation is an exhibition of this electrokinetic phenomenon. The basic cell masses in sludge, if not directly responsible for massive thrombosis, may, by additive effects, produce systemic changes in the organism.

Archives of Neurology and Psychiatry, Chicago

63:681-842 (May) 1950

Gargoylism (Lipochondrodystrophy): Study of 10 Cases, with Emphasis on Formes Frustes of Diseases. G. A. Jervis.—p. 681.
Perception of Gonadal Pain in Paraplegic Patients. E. Bors.—p. 713.
*Section of Corpus Callosum in Experimental Epilepsy in Monkey. N. Kopeloff, M. A. Kennard, B. L. Pacella and others.—p. 719.
Electromyographic Patterns in Reinnervated Muscle. M. D. Yahr, E. Herz, J. Moldaver and H. Grundfest.—p. 728.
*Phantom Limb Pain and Central Pain: Relief by Ablation of Portion of Posterior Central Cerebral Convolution. T. T. Stone.—p. 739.
Magnesium Intoxication: Absorption from Intact Gastrointestinal Tract. A. R. Stevens Jr. and H. G. Wolff.—p. 749.
Psychometric Patterns Associated with Multiple Sclerosis: I. Wechsler-Bellevue Patterns. W. C. Diers and C. C. Brown.—p. 760.
Interaction of Effects of Acetylcholine and Adenosine Triphosphate on Electrical Activity of Cat Cerebral Cortex. W. K. Jordan, D. W. Badal and R. March.—p. 766.
Anoxic Encephalopathy Following Poliomyelitis: Report of Case. A. T. Steegmann and H. V. Davis.—p. 774.

Section of Corpus Callosum in Experimental Epilepsy.—Kopeloff and his associates point out that the effect of sectioning the corpus callosum in human epilepsy remains a controversial issue. They had previously demonstrated that the application of aluminum oxide (alumina) cream to one motor cortex of the monkey induced recurrent epileptiform seizures. The onset, after a latent interval of three to twelve weeks, was characterized by contralateral jacksonian seizures. These attacks increased in severity and usually became bilateral. Because of clinical progression in the monkeys from unilateral to bilateral attacks with a corresponding spread of electroencephalographic abnormality, the present study was undertaken to determine the effect of section of the corpus callosum in monkeys (*a*) in whom bilateral seizures had been established and (*b*) in whom section had been made prior to the application of aluminum oxide cream. It was found that section of the corpus callosum either before or after the application of aluminum oxide cream caused the complete restriction of subsequent seizures to the contralateral side. The resulting unilateral attacks were considerably severer and more easily elicited than those observed in a large control series of "epileptic" monkeys with intact corpus callosum. Section of the corpus callosum after bilateral seizures had been established caused status epilepticus on the side opposite the focus in 3 of 4 monkeys, while section of the corpus callosum prior to the application of aluminum oxide cream to one cortex resulted in easily elicited contralateral seizures but not in status epilepticus. Section of the corpus callosum did not completely inhibit the spread of abnormal electrical impulses to the side opposite the focus.

Relief of Phantom Limb Pain.—Magoun stated that the posterior central convolution of the brain is one of the receptive centers for the consciousness of pain and that ablation of a specific area in the posterior central convolution should relieve pain in a specific area on the opposite side of the body. Stone gives the histories of 3 patients with phantom limb pain of organic origin and 1 (case 3) of central pain. In all 3 permanent relief was produced by subpial resection of a corresponding area in the posterior central convolution. Evidence points to the peripheral nerve stump as producing the bizarre symptoms of phantom limb. Stimuli originating at the periphery of the amputated nerves transmit these impulses by pathways to the level of consciousness. There must be three active parts: divided and exposed nerves in the stump, patent nerve pathways and a sensory cortex to receive these impulses. In order to remove such symptoms one would have to sever every nerve and its pathways from the stump to the sensory cortex concerned with consciousness. This would require considerable time and involve a tremendous risk. Relief of such symptoms could more easily be obtained by subpial resection of the area in the posterior central convolution for the extremity involved. This procedure should be limited to patients who have symptoms of the organic type of phantom limb; undue warmth; itching or distress in the phantom limb; intermittent or continuous severe burning pain; deep agonizing, torturing sensations; piercing, cramping or cutting pains, and various types of throbbing and stabbing sensations. Various other types of sensory disturbances, such as kinesthetic and tactile sensations, defects in the body scheme and postural abnormalities, are not to be treated by resection of the posterior central convolution. Posterior chordotomy or resection of the posterior columns and horns in the cervical portion of the spinal cord is the procedure for such complaints. The neurosurgeon should not perform any operation for relief of phantom limb or central pain unless he is sure that the pain is of organic nature. When this is true he should do a subpial resection of the corresponding area in the posterior central convolution. By thus affording relief to the patient he may prevent drug adiction, alcoholism or suicide.

Blood, New York

5:401-498 (May) 1950

Refractoriness in Hemophilia to Coagulation-Promoting Agents: Whole Blood and Plasma Derivatives. W. B. Frommeyer Jr., R. D. Epstein and F. H. L. Taylor.—p. 401.
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Thrombotic Thrombocytopenic Purpura: II. Studies on Hemolytic Syndrome in This Disease. K. Singer, A. G. Motulsky and J. N. Shanberge.—p. 434.
Thrombocytopenic Purpura Complicating Infectious Mononucleosis: Report of Case and Serial Platelet Counts During Course of Infectious Mononucleosis. R. M. Angle and H. L. Alt.—p. 449.
Megaloblastic Anemia of Infancy: Response to Vitamin B_{12}. P. Sturgeon and G. Carpenter.—p. 458.
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Bull. of School of Med. Univ. of Maryland, Baltimore

35:49-90 (April) 1950

Aureomycin and Chloromycetin in Treatment of Experimental and Clinical Peritonitis. G. H. Yeager, W. L. Byerly Jr., W. A. Holbrook Jr. and others.—p. 51.
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Antepartum Cephalic Molding in Rachitic Pelvis. D. F. Kaltreider.—p. 68.
Mucocele of Appendix: Review of Literature with Report of 2 Cases. J. N. Cianos, A. S. Garrison and G. A. Stewart.—p. 72.

California Medicine, San Francisco

72:337-404 (May) 1950

Case History of Uncle Sam. R. S. Kneeshaw.—p. 337.
*Newer Methods for Selection of Patients for Lumbar Sympathectomy. T. Winsor.—p. 342.
Newer Insecticides and Scabicides. C. J. Lunsford.—p. 350.
Indications for Pulmonary Resection in Infants and Children. J. C. Jones.—p. 352.
Psychiatric Problems in Children: Part 1 of Two Parts. S. A. Szurek.—p. 357.
Cholangiography Following Common Duct Drainage. C. E. Rees.—p. 363.
Early Diagnosis of Strangulation Obstruction of Small Intestine. H. P. Totten.—p. 365.
Diagnostic Problem in Asthma. J. H. Black.—p. 369.
Recent Advances in Symptomatic Treatment of Osteoarthritis. R. D. Miller.—p. 373.
Histamine and Antihistaminic Drugs. E. L. Keeney.—p. 377.

Lumbar Sympathectomy.—Winsor used pneumoplethysmograms and readings of skin temperature and skin resistance to determine the degree of vasodilatation achieved by various diagnostic methods in 98 patients with peripheral vascular disease. Arterial occlusion produced with a blood pressure cuff, ganglionic block produced with 2.6 dimethyl piperidinium bromide or tetraethylammonium ion, lumbar sympathetic block produced with 10 cc. of a 2 per cent procaine solution, spinal anethesia and indirect heating of the body by applying two double-sized electric pads, were the diagnostic methods which were compared and interpreted as to their value in determining the type of patient with vascular disease for whom lumbar sympathectomy would be of benefit. As a rule, lumbar sympathectomy was effective in patients who preoperatively had shown a positive response upon release of arterial occlusion. A negative response or absence of significant increase in blood flow does not necessarily indicate organic disease, and cannot be taken to mean that lumbar sympathectomy would be ineffective. Ganglionic block was generally less reliable in indicating the probable results of sympathectomy than lumbar sympathetic block or indirect heating. Lumbar sympathetic block was followed by a greater increase in skin temperature and blood flow than spinal anesthesia and permitted far more accurate conclusions as to the probable outcome of sympathectomy. The plethysmogram subsequent to indirect heating showed characteristic difference depending on the degree of vascular disease present. The appearance of large alpha and beta waves in the course of body heating indicates the presence of an active vasomotor response and suggests that lumbar sympathectomy may materially increase the blood flow through the digits. Conversely, the absence of these waves following body heating suggests that lumbar sympathectomy would be of little benefit. The effect of this simple safe and painless method on the relative blood flow to the toe makes it possible to arrive at a comparatively accurate estimate of the clinical benefit to be expected from lumbar sympathectomy.

Canadian J. of Research. Medical Sciences, Ottawa

28:19-68 (April) 1950. **Partial Index**

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Steroid Excretion of Infants. W. F. Perry and H. Chochinov.—p. 47.
Alkaline and Acid Phosphatase in Cerebrospinal Fluid: Data for Normal Fluids and Fluids from Patients with Meningitis, Poliomyelitis or Syphilis. K. G. Colling and R. J. Rossiter.—p. 56.

Cancer, New York

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Possible Relationship Between Menopause and Age at Onset of Breast Cancer. E. Anderson, S. C. Reed, R. A. Huseby and C. P. Oliver.—p. 410.
Tumors of Parathyroid: Review of 23 Cases. B. K. Black and L. V. Ackerman.—p. 415.
Tumors of Salivary Glands: Clinicopathological Study of 160 Cases. A. J. Rawson, J. M. Howard, H. P. Royster and R. C. Horn Jr.—p. 445.
Primary Lymphosarcoma of Small Intestine: Analysis of 13 Cases and Review of Literature. P. M. Marcuse and A. P. Stout.—p. 459.
Tracheal Aspiration—Additional Method for Early Diagnosis of Carcinoma of Lung: Preliminary Report. W. G. Cahan and H. W. Farr.—p. 475.
Prostatic Smear. H. Peters.—p. 481.
Serum Antiproteolytic Reaction of Patients with Lesions of Stomach and Duodenum. E. E. Cliffton and L. E. Young.—p. 488.
Toxic Reactions of 4-Amino-Pteroylglutamic Acid (Aminopterin) in Patients with Far-Advanced Neoplastic Disease. S. G. Taylor III, G. M. Hass, J. L. Crumrine and D. P. Slaughter.—p. 493.
Erythroblastemia: Report of Case. P. J. Fitzgerald, G. K. Mallory and F. Parker Jr.—p. 504.
Lymphangiosarcoma in Postmastectomy Lymphedema: Case Report. L. R. Ferraro.—p. 511.
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Circulation, New York

1:1073-1232 (May) 1950

Standardization of Ballistocardiogram by Simulation of Heart's Function at Necropsy: With Clinical Method for Estimation of Cardiac Strength and Normal Standards for It. I. Starr, O. Horwitz, R. L. Mayock and E. B. Krumbhaar.—p. 1073.
*Long-Term Dicumarol Therapy to Prevent Recurrent Coronary Artery Thrombosis. E. S. Nichol and J. F. Borg.—p. 1097.
*Hypothyroidism Produced by Radioactive Iodine (I^{131}) in Treatment of Euthyroid Patients with Angina Pectoris and Congestive Heart Failure: Early Results in Various Types of Cardiovascular Diseases and Associated Pathologic States. H. L. Blumgart, A. S. Freedberg and G. S. Kurland.—p. 1105.
Relation of Basal Metabolic Rate to Vasodilatation and Vasoconstriction of Extremities of Normal Subjects as Measured by Skin Temperatures. G. M. Roth and C. Sheard.—p. 1142.
Effect of Nicotinic Acid on Cerebral Circulation, with Observations on Extracerebral Contamination of Cerebral Venous Blood in Nitrous Oxide Procedure for Cerebral Blood Flow. P. Scheinberg.—p. 1148.
Myocardium in Subacute Bacterial Endocarditis. O. Saphir, L. N. Katz and I. Gore.—p. 1155.
Review of Single Coronary Artery with Report of 2 Cases. J. C. Smith.—p. 1168.
Effect of Digitalis on Clotting of Blood in Normal Subjects and in Patients with Congestive Heart Failure. R. T. Cathcart and D. W. Blood.—p. 1176.
Rate of Disappearance of Lanatoside C and Digitoxin from Blood of Rats. R. Bine Jr. and M. Friedman.—p. 1182.
Q-T Interval in Electrocardiogram of Children with Tuberculosis. T. T. Fox, H. Berger, E. Kaplan and J. C. Marshal.—p. 1184.
Coronary Arteriography in Intact Dog. F. Pearl, M. Friedman, N. Gray and B. Friedman.—p. 1188.
Heparin in Experimental Myocardial Infarction. N. B. Roberg and W. H. Requarth.—p. 1193.
Preliminary Report on Clinical Use of New Anticoagulant, Phenylindandione. A. U. Blaustein, J. J. Croce Jr., M. Alberian and N. Richey.—p. 1195.
Dicumarol Fatality in Severe Hypertensive and Arteriosclerotic Cardiovascular Disease Despite Controlled Therapeutic Level. R. E. London.—p. 1205.

Long Term Dicumarol® Therapy.—Nichol and Borg treated 78 patients who had one or more attacks of acute coronary thrombosis and/or myocardial infarction with dicumarol® given prophylactically for periods ranging from three to sixty-two months to prevent recurrent attacks. Twelve patients died, but only 4 of these had recurrent coronary thrombosis. Nine patients discontinued therapy. Fifty-seven patients remain on the regimen. They are active and doing well with little anginal complaint. Two or three years have passed without an attack in 10 of these patients, and over five years have passed since the last recurrence in 1 noteworthy patient who had three previous myocardial infarctions. Four of the living patients experienced episodes of acute coronary insufficiency with possible subendocardial infarction, followed by recovery without thromboembolic complications. One woman aged 63 and still alive had a recurrent myocardial infarction while receiving dicumarol.® Major hemorrhagic episodes occurred in 13 patients and resulted in 2 fatalities, only 1 of which could fairly be attributed to use of the anticoagulant drug. Three other patients abandoned the regimen. The remainder resumed dicumarol® treatment satisfactorily. No toxic effect on the

kidneys or liver was observed in 7 instances in which necropsy was performed after dicumarol® treatment for two to twenty-three months. Clinical evidence of such toxicity was not observed in the living patients. Great disparity in the weekly drug requirement of different patients (varying from 225 to 950 mg. per week) occurred in the course of long term dicumarol® therapy. Even more important is the sudden change in a patient's tolerance that may occur after many months of treatment with the drug. Its continuous use over a period of years to prevent recurrent coronary thrombosis is feasible and relatively safe, but no conclusions as to the efficacy of the regimen can be drawn from this small uncontrolled series.

Hypothyroidism Produced by Radioactive Iodine.—Blumgart and co-workers induced hypothyroidism by radioactive iodine in 18 euthyroid patients with advanced angina pectoris or congestive heart failure who were refractory to the standard medical measures and were seriously incapacitated. The duration of post-treatment observation was seven to twenty-four months. Each patient received orally a total of 25 to 150 millicuries of radioactive iodine in single or divided dose, of which a total of 7.3 to 39 millicuries was retained within the body during the following seventy-two hours. The largest single dose was 56 millicuries. The average total dose was 54.4 millicuries; the average three day retention was 17.9 millicuries. Neither radiation sickness nor toxic effects on the blood or kidneys were observed. Mild or moderate transitory thyroiditis occurred in 10 patients, was severe in only 1 and was absent in 7. Temporary mild hyperthyroidism occurred in 2 patients. Angina pectoris was strikingly lessened or abolished in 8 of the 13 patients with intractable cardiac pain. Concomitant congestive failure in several of the patients was likewise improved. Angina pectoris was greatly relieved in the other 5 of the 13 patients when they were myxedematous, but it recurred when thyroid was administered to ameliorate the discomfort of myxedema. Three of 5 patients incapacitated primarily because of congestive heart failure showed worth while improvement, which was striking in 2. The therapeutic procedure described should still be considered in the investigative stage. Intelligent, cooperative, emotionally stable patients between the ages of 40 and 60 with angina pectoris due to coronary arteriosclerosis, who have had frequent daily attacks on slight to moderate exertion but without any concomitant disease and have a basal metabolic rate above —10 per cent, are favorable candidates for radioactive iodine therapy. Many months of worth while existence already have been added to the lives of these disabled cardiac patients who were refractory to all standard forms of medical therapy.

GP (J. Am. Acad. of Gen. Practice), Kansas City, Mo.

1:1-128 (May) 1950

What Is New in Proctology. R. Turell and A. S. Lyons.—p. 26.
Objectives in Diabetes. E. P. Joslin.—p. 35.
Cervical Disk Protrusion. E. Neuwirth.—p. 43.
Brief Survey of Arteriosclerosis. C. F. Wilkinson Jr.—p. 49.
Obligations in Anesthesia. S. J. Martin.—p. 55.

Illinois Medical Journal, Chicago

97:233-296 (May) 1950

Post-Operative Care of Surgical Patient. M. S. Sadove and R. C. Balagot.—p. 247.
Salt Excretion in Liver Disease. J. Fershing and L. A. Baker.—p. 251.
Carcinoma of Breast. L. River, J. Silverstein, R. Tanoue and J. W. Tope.—p. 259.
Results that are Obtained in Mass X-Ray Survey. J. B. Novak and T. L. Waterman.—p. 262.
Equatorial Africa—Six Months of Adventure. C. L. Birch.—p. 265.
Strange Ways in Which the Allergic Mechanism is Altered. J. Peters.—p. 267.
Hip Disorders in Children: Differential Diagnosis. L. W. Russell.—p. 273.
Alcoholic Neuropathy and Laennec's Cirrhosis. W. Saphir and J. Spurlock.—p. 278.
Rhinophyma and Acne Rosacea Treated with Electrosection Current. W. A. Rosenberg and I. M. Felsher.—p. 281.
*Severe Anaphylactic Reaction to Wasp Sting. J. T. Paul and S. J. Presley.—p. 283.

Severe Anaphylactic Reaction to Wasp Sting.—Paul and Presley report a 58 year old man who was hospitalized 40 minutes after being stung by a wasp on the upper lip. His blood pressure and the radial pulse could not be obtained. The skin was cold, face flushed and the lips and nails cyanotic. The upper lip was edematous. Respiration was rapid, shallow and labored. Oxygen was given by mask and venoclysis of 5 per cent glucose in physiologic saline solution administered. Twenty mg. of diphenhydramine hydrochloride (benadryl) was given intravenously and 0.5 cc. of epinephrine 1:1,000 subcutaneously. A short time after a second intravenous injection of benadryl (10 mg.) was given, the blood pressure rose to 110/80. A profuse bloody diarrhea developed with the return of consciousness and continued intermittently for the next 24 hours. The symptoms gradually subsided. He was discharged 3 days later feeling well. The response to bee or wasp stings is variable. There are reports in the literature of shock-like syndrome and death within a few minutes. Severe reactions are likely to occur when the site of the sting is of high vascularity such as the lips or dorsum of the hand. Until recently severe anaphylaxis due to wasp or bee stings was treated by epinephrine. Treatment with antihistaminic drugs was suggested advisable when the histamine-like effect of the sting was recognized. It proved effective in this case.

Indiana State Medical Assn. Journal, Indianapolis

43:257-352 (April) 1950

Physician's Role in Fight Against Cancer. L. A. Scheele.—p. 277.
Intra-Epithelial Carcinoma of Cervix. D. A. Bickel and C. S. Culbertson.—p. 281.
Carcinoma of Lung. W. Carson.—p. 288.
Huggins' Test for Cancer. J. L. Eisaman, L. A. Schneider and R. E. Berger.—p. 291.

43:353-444 (May) 1950

Significance of Ocular Vascular Accidents. W. L. Benedict.—p. 369.
Sympathetic Ophthalmia: 3 Case Reports. W. M. Cockrum, H. C. Slaughter and E. U. Murphy.—p. 373.
Angiospasm (General Application). C. J. Rudolph.—p. 376.
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Industrial Medicine and Surgery, Chicago

19:213-256 (May) 1950. **Partial Index**

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Relative Infrequency of Occupational Dermatoses in Automobile Workers. J. R. Rogin and M. W. Jocz.—p. 219.
Early Detection of Benzene Toxicity. L. Blaney.—p. 227.
*Use of Radioactive Static Eliminators in a Printing Plant. I. L. Berman and E. P. Ernest.—p. 229.
Method of Reducing Accident Rate in Bus Operation: Selection of Bus Operator. H. Brandaleone and R. H. Daily.—p. 231.
Use of Intravenous Procaine in Trauma. D. J. Graubard and H. V. Spaulding.—p. 235.

Use of Radioactive Static Eliminators in a Printing Plant.—According to Berman and Ernest static electricity is generated by the movement of paper over rollers in printing presses and in paper folding machinery. In addition to control of temperature and relative humidity of the work room, gas flame, high-voltage electricity and tinsel have been used to eliminate or neutralize static in printing processes. Recently, radioactive materials have entered this field. Eliminators utilizing radium emit alpha particles, and beta and gamma rays as well as radon gas, all of which present a health hazard. The authors describe studies made on radioactive static eliminators made in a U. S. Government Printing Office. The installations were checked with radiation detection devices. Readings of combined beta and gamma radiation indicated an exposure of from 3 to 5 mr/hr. at positions which are considered normal for pressmen and helpers. Although the instruction manual stressed the importance of replacing the cover plate when the press was not in operation, no effort was made to do so. The authors cite figures on maximum permissible exposure, which indicate the need of shields and other precautions to protect the workers against the hazards of exposure to radioactive material. The brackets attaching the static eliminators to the presses should be installed to permit the use of the cover plates. A quick acting attaching device should be used. The shields should be affixed to the unit when the helper is washing up, or when the pressman is in the space between the press and the delivery assembly, or when maintenance personnel enter this space. The radioactive units should be removed and placed in a properly guarded place, whenever a worker has to be for more than an hour within 20 inches of the site of attachment of the units. Gloves should be worn when cleaning the active surface of the eliminator.

Maine Medical Association Journal, Portland

41:93-122 (April) 1950

Repair of Ventral Hernia with Tantalum Gauze in Dibilitated and Tissue Deficient Patient. A. H. McQuillan.—p. 93.
Transitional Cell Carcinoma of Renal Pelvis—Case Report. J. F. Reynolds and I. I. Goodof.—p. 95.
Purpura—Case Report. G. J. Robertson and I. I. Goodof.—p. 97.
Present Day Prognosis in Idiopathic Detachment (Separation) of Retina, and Causes of Failure. H. F. Hill.—p. 99.
Neonatal Mortality with Reference to Anoxic Injury. E. N. Ervin.—p. 101.
Treatment of Cerebral Vascular Accidents. G. J. Robertson.—p. 104.
Infectious Mononucleosis—Brief Review. F. B. Champlin.—p. 105.
Allergy of Middle Ear. S. Fisher and F. T. Hill.—p. 107.
Complications of Whole Blood Transfusion and Immediate Treatment. V. J. Moore.—p. 108.
Epistaxis. L. W. Pratt.—p. 111.

Michigan State Medical Society Journal, Lansing

49:358-496 (April) 1950

Types of Diabetes Mellitus and Their Treatment. A. R. Colwell.—p. 417.
Scalp Traction of Management of Cephalic Presentation with Hydrocephalus. M. M. Rozan.—p. 426.
Rickettsial Disease in Michigan: Report of 2 Cases. C. J. Smyth.—p. 427.
Uterogram in Sterility. R. C. Hildreth and C. P. Chrest.—p. 431.
Pregnancy and Labor Experiences of Elderly Primigravidas. E. G. Walters and H. P. Wager.—p. 435.
Leukemia in Pregnancy. E. G. Murphy and R. E. Johnson.—p. 439.
Corneal Transplantation. M. Croll and L. J. Croll.—p. 442.
*Chloromycetin as Treatment for Pertussis: Continued Observations. E. H. Payne, M. Levy, E. Zabalaga Canelas and others.—p. 450.
Chickenpox and Herpes Zoster: Simultaneous Occurrence in Same Patient. E. H. Watson.—p. 452.
Histamine Antagonists: XVII. Experimental and Clinical Experience with N,N-Methyl-N'-(4-Fluorobenzyl)N'-(2-Pyridyl)-Ethylenediamine. S. M. Feinberg.—p. 454.
Primary Inflammatory and Ischemic Disease of Appendices Epiploicae. T. Wilensky.—p. 458.

Chloramphenicol® in Pertussis.—Payne and his associates report additional experience gained in the treatment of pertussis with chloramphenicol (chloromycetin®). The majority of the cases reported were treated in the Department of Cochabamba, Bolivia. The epidemic during which this study was made began late in June and continued through November 1949. The death rate of untreated patients under 5 years of age was 20 per cent. Treatment with high potency vitamins gave some amelioration but had no curative effect. Penicillin and streptomycin were of some aid in controlling the complications but of doubtful value in shortening the disease. Since the supply of chloramphenicol was limited and there was such a large number of patients, only those who were seriously ill received the antibiotic. The diagnosis was confirmed by cough plate or swab cultures. Sixty-two patients were treated. Chloramphenicol was given in varying doses, depending on the weight of the child, and was administered orally in most cases. The drug was given to some as a rectal suppository or as an intravenous injection dissolved in propylene glycol. The total dose in infants less than 1 year old was usually around 2 Gm. It varied in older children between 3 and 9 Gm. Fever usually subsided during the second day, and paroxysms usually disappeared between the third and sixth days of treatment. The authors conclude that chloramphenicol is effective against pertussis.

New Orleans Medical and Surgical Journal

102:525-590 (May) 1950

Use of Intravenous Procaine in Treatment of Arthritis. J. R. Green, A. A. Doerner and E. M. Gordon.—p. 525.
Viral Hepatitis: Report of 2 Cases Treated with Chloramphenicol. H. Lott, R. W. Young and J. C. Stovall.——p. 528.
Uncomplicated Gastric and Duodenal Peptic Ulcer. G. G. McHardy and D. C. Browne.—p. 529.
Congenital Malrotation of Midgut in Infants: Report of 4 Cases. B. C. Garrett and L. J. O'Neil.—p. 539.
Changing Picture in Appendiceal Disease: Fifteen Year Survey at Touro Infirmary. G. N. Weiss.—p. 542.
Cardiac Predecompensation. E. Hull.—p. 549.
Treatment of Common Cold. O. W. Bethea.—p. 554.
Oculoglandular Tularemia. J. W. Rosenthal.—p. 558.
Value of Hearing Clinic: Present Policies and Long-Term Objectives of Hearing Clinic at Eye, Ear, Nose and Throat Hospital in New Orleans. L. W. Alexander.—p. 566.
Public Health Aspects of Decreased Hearing in Children. J. D. Martin.—p. 575.

Rocky Mountain Medical Journal, Denver

47:325-404 (May) 1950

Irritable Bowel Syndrome. P. W. Brown.—p. 343.
Postpartum Hemorrhage. H. S. Morgan.—p. 347.
Treatment of Carcinoma of Cervix. A. N. Arneson.—p. 350.
Traumatic Facial Paralysis with Case Report. G. B. Flagg.—p. 355.
Fascia Lata Sling for Facial Paralysis: Improved Technic. D. W. Macomber.—p. 357.
*Treatment of Pruritis Ani with Para Nitrophenol and Sodium Iodate. H. K. Belnap.—p. 361.
G. P.—Step-Child of Medicine? A. H. Gould.—p. 364.
Common Malignant Tumors of Ocular Adnexa. C. S. O'Brien.—p. 367.

Treatment of Pruritus Ani.—According to Belnap pruritus ani may be caused by bacterial, fungous or trichomonal infection. It may also be due to a neurosis, to syphilis, the menopause, genitourinary disease, pregnancy, hepatic disease, diabetes or allergy. Belnap reports on 100 cases in which the laboratory isolated a fungus from scrapings of the perianal tissues. The fungi isolated most frequently were the epidermophyton and trichophyton. The anal canal was examined for other pathologic conditions. If associated cryptitis or papillitis was found, the following treatment was instituted: sulfathalidine by mouth for a period of ten days; sulfadiazine cream injected into the rectum twice daily; sitz baths twice daily, and mild laxative agents to produce a soft stool. The perianal skin was treated with a preparation consisting of paranitrophenol and sodium iodate in isopropyl alcohol, to which had been added substances which act as wetting agents. Treatment with this compound effected cure in 91 of 100 cases; 5 patients had a recurrence, and 4 failed to respond.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

58:205-256 (May) 1950

Immediate Treatment of Burned Child. W. S. Kiskadden and A. McDowell.—p. 205.
Osteoid-Osteoma. F. M. McKeever.—p. 213.
Intertrochanteric Fractures of Hip. O. Neufeld, T. M. Mulford and C. Steggall.—p. 219.
Manual Osteoclasis for Treatment of Bowleg Deformities. A. Brockway.—p. 221.
Sickle-Cell Anemia Complicated by Pregnancy. R. R. Maier and M. Klein.—p. 224.
New Vaginal-Abdominal Hysterectomy with Special Knife. M. Joseph.—p. 227.
*Adrenocorticotropic Hormone (ACTH) in Etiology of Eclampsia. S. S. Garrett.—p. 229.
Treatment of Vaginitis. E. D. Lawrence.—p. 236.
Use of Male Bufo Marinus Toad in Diagnosis of Pregnancy. M. D. Bivens.—p. 238.
Therapeutic Use of Rocker Sole. C. L. Lowman.—p. 243.

Pituitary Adrenocorticotropic Hormone and Eclampsia.—Garrett directs attention to the striking parallels between the results of pituitary adrenocorticotropin (ACTH) administration and the changes seen in eclamptic toxemia. He shows that administration of either anterior pituitary hormone or 11-desoxycorticosterone produces renal damage identical with that of eclampsia, the condition in both cases being characterized as a nephrosclerosis. There is close similarity in the heart, brain and liver between the lesions of eclampsia and those resulting from corticosteroids. When an eclamptic patient dies in shock the adrenals show necrosis and hemorrhage, apparently caused by ACTH overstimulation. The terminal fall in blood pressure is explained as being due to cortical failure. Before severe kidney damage can be produced in rats by corticosteroids or pituitary hormone the renal reserve must be lowered (unilateral nephrectomy) and an excess of sodium chloride administered (one per cent sodium chloride in the drinking water). Lowered kidney reserve predisposes to development of eclamptic toxemia; high sodium chloride intake aggravates the condition. Women with eclampsia show an increased excretion of corticosteroids. Following ACTH injection there is a marked rise in urinary 17-ketosteroids and 11-oxysteroids. Hypertension, edema, convulsions, and coma seen in eclampsia can be reproduced using adrenal steroids and sodium chloride. It is concluded that hyperactivity of the anterior pituitary with increased secretion of pituitary adrenocorticotropic hormone (ACTH) is the primary etiologic factor in a large percentage of patients with eclamptic toxemia.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted.
Single case reports and trials of new drugs are usually omitted.

British Heart Journal, London

12:101-212 (April) 1950

Relation Between Heart and Joint Disease Including "Rheumatoid Heart Disease" and Chronic Post-Rheumatic Arthritis (Type Jaccoud). E. G. L. Bywaters.—p. 101.
*Atebrin in Paroxysmal Tachycardia and Paroxysmal Auricular Fibrillation. F. Vega Diaz.—p. 132.
RS-T Pattern Associated with Myocardial Injury. E. Goldberger.—p. 141.
Congenital Heart Disease Associated with Subdiaphragmatic Lateral Heterotaxy. J. Thomson.—p. 147.
*Cardiac Catherization in Diagnosis of Congenital Heart Disease. H. E. Holling and G. A. Zak.—p. 153.
Radiological Features of Enlarged Bronchial Arteries. M. Campbell and F. Gardner.—p. 183.

Quinacrine in Paroxysmal Arrhythmias.—Vega Diaz points out that Gertler and co-workers have presented since 1946 several reports on the use of quinacrine hydrochloride in the treatment of paroxysmal tachycardia. He reports 6 patients to whom quinacrine was given in doses similar to those employed by Gertler. Four of the 6 patients had paroxysmal auricular fibrillation; 1 had infranodal paroxysmal tachycardia, and 1 had variably occurring paroxysmal auricular flutter. The drug was injected either intramuscularly or intravenously. In 4 patients (2 with paroxysmal tachycardia and 2 with paroxysmal auricular fibrillation) the bouts were stopped in a striking manner. In the other 2 the drug proved ineffective, although in 1 patient with paroxysmal auricular flutter the result was difficult of interpretation. Quinacrine seems to be a useful medicament, especially in patients with a high basal metabolic rate or slight hyperthyroidism. It may be less dangerous than quinidine, although possibly less potent and less efficacious when repeated. Quinacrine in therapeutic doses is not toxic for the myocardium whereas with quinidine there is only a small margin between therapeutic and toxic doses. The effects of quinacrine are slow and general rather than cardiac. Considerable retention of the drug in the system suggests that it may be useful for maintenance and prophylactic treatment. Further experiences must be awaited before final evaluation is possible.

Cardiac Catheterization in Congenital Heart Disease.—Holling and Zak practiced cardiac catheterization in 70 patients with a wide range of cardiac malformations. Cardiac catheterization is not without danger in congenital heart disease. Six of the 70 patients manifested signs indicative of pulmonary or systemic thrombosis or embolism. One patient died. The differences in oxygen content of blood obtained from the vena cava, right atrium, right ventricle and pulmonary artery are discussed in relation to the diagnosis of septal defects and patent ductus arteriosus. In the absence of intracardiac shunts and patent ductus arteriosus the oxygen content of right atrial blood should not exceed (*a*) that of the superior vena cava by more than 2 volumes per cent, (*b*) that of inferior vena caval blood by more than 3 volumes per cent or (*c*) that of the mean of superior and inferior vena caval blood by more than 2 volumes per cent. The oxygen content of right ventricular blood should not exceed that of right atrial blood by more than 1 volume per cent. The oxygen content of pulmonary artery blood should not exceed that of right ventricular blood by more than 0.5 volume per cent. Cardiac catheterization is considered in the diagnosis of the following conditions: tetralogy of Fallot, Eisenmenger's complex, transposition of the great vessels, pulmonary stenosis with closed ventricular septum, tricuspid and pulmonary atresia, truncus arteriosus, atrial and ventricular septal defects, Lutembacher's syndrome, patent ductus arteriosus and pulmonary hemangioma. The information obtained by cardiac catheterization and angiocardiography are proving valuable, the more so, because observations by these means are often complementary. Angiocardiography gives more anatomic, cardiac catheterization more physiologic information. Cardiac catheterization provides an indication whether surgical measures are necessary and whether a pulmonary-systemic anastomosis or a valvulotomy would be more useful.

British Medical Journal, London

1:919-972 (April 22) 1950

Vitamin B_{12} and Folic Acid in Megaloblastic Anaemias of Pregnancy and Puerperium. C. C. Ungley and R. B. Thompson.—p. 919.
Vitamin B_{12} in Macrocytic Anaemia of Pregnancy and Puerperium. J. C. Patel and B. R. Kocher.—p. 924.
Cases of Hypopituitarism. R. T. Cooke and H. L. Sheehan.—p. 928.
Myxoma of Left Auricle. P. M. McAllen.—p. 932.
Stilboestrol in Out-Patient Treatment of Sexual Offenders: Case Report. J. Bierer and G. A. van Someren.—p. 935.
Early Rising for Puerperal Women. A. B. Swarbreck.—p. 936.
*Two Successful Post-Mortem Caesarean Sections Following Spinal Analgesia. A. H. C. Walker and S. Matthews.—p. 938.

Successful Postmortem Cesarean Section.—Walker and Matthews describe 2 cases of maternal death after spinal analgesia, in which live babies were delivered by postmortem cesarean section. Both women were West African natives. The authors believe that risks of spinal anesthesia are peculiar to parturient women, particularly to West African pregnant women whose average blood pressure is lower, with the result that the margin of safety is less should a fall in blood pressure occur as a result of the spinal analgesic. Moreover, West Africans are often admitted late in labor in an exhausted condition and suffering from malnutrition and anemia.

Lancet, London

1:745-792 (April 22) 1950

The Open Wound in Trauma. P. Essex-Lopresti.—p. 745.
Idiopathic Steatorrhoea (Non-Tropical Sprue) with Megaloblastic Anaemia. M. C. G. Israëls and J. Sharp.—p. 752.
Vitamin B_{12} in Idiopathic Steatorrhoea. I. M. Tuck and N. Whittaker.—p. 757.
Action of Benzodioxane in Man: Experimental Investigation. F. T. G. Prunty and H. J. C. Swan.—p. 759.
Iodine an Aid to Lactation. R. F. A. Dean.—p. 762.
Transillumination of Whitlows of Terminal Phalanx. E. P. Samuel.—p. 763.

Medical Journal of Australia, Sydney

1:253-284 (Feb. 25) 1950. **Partial Index**

Clinical Management of the Premature Infant. K. Campbell.—p. 253.
Statistical and Public Health Aspects of Prematurity. B. Meredith.—p. 258.
Premature Labour. D. F. Lawson.—p. 262.
Traumatic Psychoneurosis. P. G. Dane.—p. 266.

1:285-316 (March 4) 1950

Stages in Development of Operative Surgery of Prostatic Obstruction. H. S. Newland.—p. 285.
Procaine Penicillin: Its Effectiveness in Maintaining Blood Levels, and Its Use in Treatment of General Paralysis of the Insane. I. Martin.—p. 292.
Some Everyday Problems in Dermatological Practice. W. C. T. Upton.—p. 295.
Primary Malignant Tumours of Bone. H. Platt.—p. 297.

South African Medical Journal, Cape Town

24:205-224 (March 25) 1950. **Partial Index**

Restoration of Hearing in Chronic Middle Ear Suppuration. R. T. Raymond-Jones.—p. 205.
*Standard Operation for Hypertension. A. L. McGregor.—p. 210.

Standard Operation for Hypertension.—McGregor says that since operation is accepted as part of the treatment of essential hypertension, a standard operation for this purpose should be within the scope of the general surgeon. He describes such an operation, which is basically the Smithwick operation and should be so called, although certain departures from the originator's technic have been developed in the light of experience. Male patients must be informed that they will probably be sterile following these operations, though potency is not usually impaired. Maximum safety to the patients is secured by generous exposure, an extrapleural procedure and a subtotal splanchnicectomy. The Smithwick operation of lumbodorsal splanchnicectomy fulfils these criteria.

Archives des Maladies du Coeur, Paris

42:1149-1244 (Dec.) 1949. **Partial Index**

Effect of Mercurial Diuretic on Blood Pressure of Right Heart Chambers in Cardiac Patients. L. Scébat, P. Maurice and J. Lenègre.—p. 1149.
Contribution to Study of Negativity of T3 Wave. Second Part. Clinical and Experimental Study. A. van Bogaert, A. van Genabeek and A. P. Nyssens.—p. 1157.
*Resection of Preaortic Plexus in Angina Pectoris. G. Arnulf.—p. 1191.
*Survival of Patient with Blue Disease (Type Fallot) to Age of 55 Years. C. Lian and J. Fleury.—p. 1209.

Resection of Preaortic Plexus in Angina Pectoris.—According to Arnulf, section of the preaortic plexus in dogs is compatible with life. The heart resumes its normal rhythm after the intervention. Reactions to mechanical or electrical excitation of the visceral pericardium disappear or become attenuated. Section of the preaortic plexus in dogs usually produced intense vasodilatation. Two procedures are possible in patients with angina pectoris, infiltration or resection. Infiltration of the preaortic plexus with 20 or 30 cc. of an anesthetic solution must be repeated seven or eight times to obtain a permanent sedation. The author suggests a series of 12 infiltrations and a repetition of infiltration if new attacks occur. Patients with coronary thrombosis reacted well but the infiltrations did not suffice for a prolonged sedation. Patients without coronary thrombosis recovered after several series of infiltrations. Patients who did not obtain relief from a bilateral stellectomy obtained satisfactory relief from the infiltrations. Infiltration of the periaortic plexus may be combined in refractory cases with infiltration of the stellate ganglions. Infiltration of the preaortic plexus should precede resection and serve as a test for the latter. Resection of the preaortic plexus was performed on 6 patients. The attacks were suppressed in 3. The precordial pain, the epigastric pain and the persistent pain in the arms disappeared in 1 patient; treatment failed in 1 patient and 1 patient obtained relief only for several days. This patient had coronary thrombosis and only one branch of the plexus was cut. This case demonstrates that the entire preaortic plexus must be resected including all the nervous fibers inside the pneumogastric nerve.

Survival of Patient with Blue Disease.—Lian and Fleury report a woman aged 55 who was in deep coma when admitted to the hospital. She presented dyspnea with stertor, pronounced cyanosis of the face and extremities, bilateral Babinski's sign without manifest hemiplegia, edema of the lower extremities and of the hands. The temperature was 104 F. Death occurred within several hours. Necropsy revealed an intraventricular communication associated with stenosis of the pulmonary artery and patent ductus arteriosus. Diagnosis of tetralogy of Fallot was thus established by the necropsy. History revealed that the patient had cyanosis and dyspnea on exertion since childhood. She could never play or run. Her condition improved after puberty and she was able to work as a seamstress. Impairment became worse at the age of 40. It is emphasized that the patient lead a quiet life and did not get married. Pregnancies would undoubtedly have shortened her life. The authors' case of survival to the age of 55 is next to the single case of survival to the age of 60 years reported by White and Sprague in 1929.

Medicina, Buenos Aires

10:1-76 (Feb.) 1950. **Partial Index**

*Basophilic Degeneration of Myocardium. O. C. Croxatto and J. Chiriboga.—p. 8.

Basophilic Degeneration of Myocardium.—Croxatto and Chiriboga studied the myocardium of 193 persons who died from an accident or from pulmonary tuberculosis, from acute disease of lungs or from cancer of the lung. The myocardial segment studied was taken from the left ventricle, including the wall of the auricle and the mitral valve. Basophilic degeneration of myocardium of variable degree was observed in 16 cases. The microscopic features of myocardial fibers in basophilic degeneration differentiate these lesions from those caused by autolysis. Basophilic degeneration consists of a basophilic substance located near the nucleus of the myocardial muscle fiber. This substance invades the myocardial muscle fibers and causes injury to the nuclei and breaking up of myofibrils. In sections stained with methyl-pyronine-green stain, before condensation of the basophilic substance takes place, the material stains red in the first stage of basophilic degeneration and green in the second stage. After condensation has taken place, the sections stained with hematoxiline-eosine show basophilic granules similar to calcium granules. The location of the first lesion and the behavior of microscopic sections to methyl-pyronine-green stain suggest that this type of myocardial degeneration is caused by a metabolic disorder of the sarcoplasm of the nuclei of the myocardial fibers by which ribonucleic acid of the nuclei of the fibers is liberated and is later transformed into desoxyribonucleic acid. Basophilic degeneration has no relation to atrophy and diseases of the thyroid gland or to the number of hours which have passed between death and the necropsy.

Nordisk Medicin, Stockholm

43:403-450 (March 10) 1950. **Partial Index**

Chemotherapeutics and Antibiotics in Tuberculosis. A. Westergren.—p. 403.
Primary Thoracoplasty. K. Rogstad.—p. 405.
Complications in Thoracoplasty and Their Significance in Primary Thoracoplasty. R. Christophersen, F. Lund-Johansen and A. Spilling.—p. 411.
Does Roentgenologically Demonstrable Primary Tuberculous Affection Occur as Late Manifestation of Change in Tuberculin Reaction? G. Hertzberg and L. Riddervold.—p. 415.
Pneumothorax Treatment of Primary Tuberculosis. K. Rambøl and D. Frimanslund.—p. 418.
Two Years of Tuberculin Testing and BCG Vaccination in Rural District. J. Myren.—p. 422.
Reliability of Negative Results of Gastric Lavage. K. Kristoffersen.—p. 429.
*Determination of Streptomycin Concentration in Spinal Fluid in Tuberculous Meningitis. P. Hanssen and C. Lerche.—p. 430.
Prophylactic Vasectomy in Urogenital Tuberculosis. O. Obrant.—p. 431.
Familial Occurrence of Pulmonary Geotrichosis. G. Sundgaard, T. Thjøtta and K. Urdal.—p. 434.

Streptomycin Level in Spinal Fluid in Tuberculous Meningitis.—Hanssen and Lerche made 621 biologic determinations of the streptomycin concentration in the spinal fluid of 20 patients with tuberculous meningitis treated in Ullevål Hospital since September 1948. They found an apparent correlation between the streptomycin concentration in the spinal fluid and the severity of the disorder; low values were constant in patients with clinical recovery after combined intramuscular and intraspinal or intramuscular injections of streptomycin, while values were far higher during the course of the disease in the patients who died. Determinations of the streptomycin concentration in the spinal fluid seem to be of prognostic and possibly of diagnostic value, but afford no indication as to dosage and method of treatment.

Zentralblatt für Chirurgie, Leipzig

74:785-896 (No. 8) 1949. **Partial Index**

Therapeutic Exercise and Sport for the Physically Handicapped as Part of Clinical Treatment. K. Siehlow.—p. 787.
Auxiliary Operation in Irreparable Combined Paralysis of Median and Ulnar Nerves. F. Scheffel.—p. 800.
Early Transplantation of Tendon in Radial Paralysis. H. Herbig.—p. 804.
Stiffness of Knee Due to So-Called Quadriceps Contracture. A. W. Fisher.—p. 844.
*Presacral Infiltration with Procaine Hydrochloride for Sciatica and for Painful Sciatic Nerve Due to Prolapse of Intervertebral Disk. A. Stender.—p. 833.

Presacral Infiltration with Procaine Hydrochloride for Sciatica.—Stender says that the method he employs was first described by Pendl in 1934. The object is to flood the space between the rectum and the sacrum with 150 cc. of a 0.25 per cent solution of procaine hydrochloride, because the roots of the sciatic nerve emerge on the inner surface of the sacrum. A needle 15 cm. in length is introduced in the direction toward the sacral foramens. Flooding of the sacrum with procaine hydrochloride causes the pain to subside immediately. The leg feels numb and lame for two or three hours, but after that it can be moved again. The pain is now either greatly reduced or has completely disappeared. Only in a few cases was there no effect at all. Presacral flooding with procaine hydrochloride according to Pendl's method is helpful not only in true sciatica but also in mild forms of ischialgia in connection with a prolapse of the intervertebral disk. It is ineffective in severe cases. Thus the method is important for the differential diagnosis and may make a myelogram superfluous.

BOOK NOTICES

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

Speech Therapy for the Physically Handicapped. By Sara Stinchfield Hawk. Cloth. $4. Pp. 245, with illustrations. Stanford University Press, Stanford University, California; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, 1950.

Working on the principle that most physically handicapped persons have speech defects which provide additional handicaps and that most persons with speech defects have physical and emotional handicaps as well, Sara Stinchfield Hawk describes the total approach to speech therapy in the Orthopedic Hospital at Los Angeles. The medical background for this concept is developed in an introduction by Dr. Charles Leroy Lowman.

To obtain the best results, the training of the speech mechanism cannot be undertaken independently of that of other muscular systems. To secure reasonable fluency in the creation of ideas and speech a child should be free from abnormal fears, excessive inhibitions, timidity, shrinking and feelings of inferiority and insufficiency stemming from his handicap.

In the chapter on clinical methods, which covers more than half the book, the details of acceptable case history are outlined and explained; technics for relaxation preliminary to speech therapy are presented, and considerable information is given on word exercises. Much of the speech training recommended is associated with action exercises in which simple gesture as well as attempts at spontaneous dramatization are stressed as an assistance to the emotional and physical factors in the production of coherent speech.

A chapter on research summarizes in considerable detail 53 clinical cases gleaned from reexaminations of a group of 175 speech patients who have been treated over an eight year period. This gives a fair concept of the kind of clinical material on which the author's concept of speech correction is based. An appendix on personality measurement and vocational guidance describes the comparative usefulness of most of the technics of personality measurement and describes ways and means of using vocational guidance for speech improvement. It also describes the effect security of occupation has on physically handicapped persons with speech defects. A bibliography is included.

This volume should be useful to speech clinicians and to all, regardless of their profession, who may be concerned with physically handicapped persons, particularly children.

The Normal Sex Interests of Children from Infancy to Childhood. By Frances Bruce Strain. Cloth. $2.75. Pp. 210, with 1 illustration. Appleton-Century-Crofts, Inc., 35 W. 32d St., New York 1, 1948.

With a reader appeal including parents, all teacher levels from kindergarten to college, psychologists, child nurses and play leaders, this book is another gentle nudge, or perhaps a forthright push, in the direction of more natural sex education for children. The author, who has built up a commendable reputation in this field with her earlier books, such as "Being Born" and "Love at the Threshold," is refreshingly calm and matter of fact in her discussions. Even though some parents may have personal feelings that prevent full acceptance and application of certain of the instruction technics, many others will find new support for a courageous solution of the sex education dilemma as it occurs and recurs in the family circle.

Although the title indicates that the top level is childhood, in the latter part of the book there is considerable discussion of sex interests and problems of adolescence. In an introductory chapter the author provides an instructive review of the problems that for so many years kept sex education denied and suppressed and offers encouraging evidence of the healthful changes that have taken place and, in her opinion, will continue to take place. An interesting chapter is one containing observation records of manifestations of sex interest in infancy, preschool, primary, elementary, junior and senior high school boys and girls, with a sample chart blocked out for parents and teachers. Detailed consideration of developmental attitudes is given in chapters on infancy, the preschool period, the preadolescent personality, boy and girl interests in preadolescence, changes at puberty and social and psychic interests in adolescence. This book can be recommended to parents and others whose contacts are with children at the various stages of physical and social development that are so important and are still much neglected.

Sexual Deviations. By Louis S. London, M.D., and Frank S. Caprio, M.D. With a Foreword by Nolan D. C. Lewis, M.D., Professor of Psychiatry, College of Physicians and Surgeons, Columbia University, New York. Cloth. $10. Pp. 702. The Linacre Press, Inc., P. O. Box 2606, Washington 6, D. C., 1950

This book satisfies the genuine need for a comprehensive treatise on psychosexual pathology. The authors present a short survey of the theoretic background, then give histories of patients whom they have observed in their practice of psychoanalysis, with special emphasis on the psychodynamics of each sexual deviation. Finally, the therapeutic and social aspects of these disorders are discussed. A good glossary of terms and a useful bibliography are included in the book.

The rich material collected by the authors is presented in an excellent way. The reader will certainly follow with interest many of the cases, especially that of a lesbian whose dreams were analyzed by Dr. Caprio without his knowledge of the patient, of her anamnesis or her reaction to her analyst, Dr. London. The entire book is written in the tradition of Freud and Stekel, who contributed so much to the knowledge of sexual pathology. Physicians and criminologists will appreciate the concise analyses and the optimistic outlook of this volume, which reassures them that psychic conditions can and must be treated by psychic methods.

Community Health Organization. By Ira V. Hiscock, M.P.H., Sc.D., Chairman, Department of Public Health, Yale University, New Haven. Fourth edition. Cloth. $2.75. Pp. 278. The Commonwealth Fund, Division of Publications, 41 E. 57th St., New York 22; Oxford University Press, Amen House, Warwick Sq., London E.C.4, 1950.

Since its first appearance, in 1927, this book has been standard as a textbook and reference work. The author, who is chairman of the Department of Public Health at Yale, has grown up with public health progress during the past quarter-century and is thoroughly versed in all its ramifications. The book gives a complete basis for understanding of modern public health work, both official and voluntary, in American community life, together with organization tables, qualifications of personnel, salaries and other costs and per capita expense to the taxpayer. The book is an essential item in every public health library and should be useful for practicing physicians serving on medical society committees having to do with public policy, public relations, public health and the growing movement toward community health councils. Professor Hiscock, though not a physician, has been noted throughout his career as one keenly mindful of the appropriate place for the doctor in the public health picture.

Fundamentals of Pharmacy, Theoretical and Practical. By Walter H. Blome, Ph.C., M.S., M.A., and Charles H. Stocking, Ph.C., M.S., Dean, University of Michigan College of Pharmacy, Ann Arbor, Mich. With Contributions by Elmon L. Cataline, Ph.D., Robert L. Jones, Ph.C., M.S., and Edward C. Watts, B.S. Second edition. Cloth, $5. Pp. 312, with 158 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1949.

This text is intended for the beginning student of pharmacy who has little preparation in the basic sciences. It is to be used in the study of the fundamental principles and practices of pharmacy. It consists of two parts, the first dealing with the

theoretic nature of pharmacy, the second with the practical aspects of the subject. Each of the 37 chapters is concluded with a brief bibliography of standard references to the subject covered. Compared with related texts, it is more compact but requires supplementary material. The last four chapters of the text concern biologic preparations, animal products, vitamins, homeopathic pharmacy and hospital pharmacy. Their inclusion in an elementary textbook is of doubtful value. There are numerous illustrations, but so many are outmoded and antiquated that a student would not get much help from them. There are errors in the theoretic portion of the text. The entire chapter on specific gravity should be more carefully written and the related concepts more clearly defined. The chapter on precipitation may be confusing to the student. Specific errors are observed in the definitions of isoelectric point, sublimation and hydrates. Pectin pastes are not mentioned, and the chapter on ointments is inadequate as it fails to include the factors which affect the availability of active ingredients from this type of preparation. The confusing nature of the material, the errors in part I and omissions in part II detract seriously from its usefulness. The printing is good and on high gloss paper.

Papers Dedicated to Dr. Poul Iversen on His Sixtieth Birthday, November 20, 1949. Accompanies Vol. 136, Acta medica Scandinavica, Supplementum 234. Paper. Pp. 339, with illustrations. Rosenkilde and Bagger, Copenhagen, 1949.

Dr. Poul Iversen, physician in chief, Third Medical Department, Kommunehospitalet, Cophenhagen, should feel proud of the progress and work of his many pupils. As a clinical teacher he established one of the few "scientific schools" in Sweden. As a tribute to their teacher and colleague, his students and associates have published a memorial supplement to *Acta medica Scandinavica* which contains 43 papers on a wide variety of clinical and laboratory problems in medicine. Most of these papers are written in English; a few are in German.

The publication of tributes of this sort to outstanding teachers is a nice gesture of respect and affection, particularly when it is done at a time when the recipient can appreciate it.

Medizin in Bewegung: Klinische Erkenntnisse und ärztliche Aufgabe. Von Richard Siebeck, Dr. med., o. Professor und Direktor der Ludolf-Krehl-Klinik Heidelberg. Cloth. Pp. 520. Georg Thieme, Diemershaldenstrasse 47, Stuttgart-O, 1949.

This volume is a clinical-philosophic recital of the progress of internal medicine. The work is the result of the author's extensive clinical experience. Throughout, the author insists on a "psychosomatic" approach. However, the vagueness of the term becomes evident as one reads the various chapters. It appears that most patients with peptic ulcer have a history of emotional conflicts and a labile vegetative nervous system. The author admits that this is not true of all ulcer patients. The point is particularly stressed in the case of thyrotoxicosis. The only inference the reader can make from these observations is that the treatment of a patient with an ulcer or with thyrotoxicosis should be individualized. In spite of the emphasis on psychosomatic medicine one finds the orthodox therapeutic regimens and the customary drugs in the treatment of these diseases. It is interesting to note that in the first chapter of the book, which is devoted to a brief review of the growth of medicine, there is an account of Freud and of psychodynamics. However, the influence of this new discipline does not become apparent either in the discussion of the etiology of various diseased states or their treatment.

Lord Lister: His Life and Doctrine. By Douglas Guthrie. Cloth. $3.50. Pp. 128, with 21 plates. Williams and Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1949.

One of the best known figures in medical history is Joseph Lister. His contributions, which revolutionized the practice of surgery, have been the subject of many articles. Few who are familiar with his work or who are interested in famous medical figures will be disappointed in the eight chapters of this new book. Discussions of surgery before Lister, Lister as a student with Prof. James Syme, the discovery and practical application of the antiseptic principle and other interesting aspects of Lister's life are skilfully and invitingly offered to the readers. Lister's admirers and students of medical history will welcome this contribution. The printing and reproductions are satisfactory. The index is informative.

How to Be Happy Though Young: Real Problems of Real Young People. By George Lawton. Cloth. $3. Pp. 300. The Vanguard Press, Inc., 424 Madison Ave., New York 17, 1949.

This is a well written, straightforward presentation based on "real problems of real young people," as stated on the title page. It proceeds in a logical manner, starting with the problem of getting along with oneself. Based on letters or questions, many of the former published and answered over a ten year period in *Scholastic* magazine, this discussion deals with moods, memories "that are too real," fears, shyness, "blues," who is "in charge of yourself," "can people be remade," daydreams, lonesomeness, dream interpretation (sensibly done) and the "well adjusted person." In like manner, subsequent chapters or sections are devoted to how to get along with one's family, how to get along with other persons, the opposite sex, friends, a career, school, society and the universe. There are three interesting, useful, and sometimes a bit pungent, appendixes, entitled, What Do Boys and Girls Really Worry About, Youth's Bill of Rights and Phrases to Which Young People Are Allergic. All this book, especially the last appendix, would make useful if not always comfortable reading for any parent. Doctors dealing with young persons and their parents can recommend this book with confidence and would not be wasting their time if they read it themselves.

Famous Men of Medicine. By Caroline A. Chandler, M.D. Cloth. $2.50. Pp. 140, with 18 illustrations. Dodd, Mead & Company, Inc., 432 Fourth Ave., New York 16, 1950.

This is essentially a primer for lay persons. Pictures and brief discussions may be found on Hippocrates, Galen, Arabian physicians, Vesalius, Paré, William Harvey, Edward Jenner, Elizabeth Blackwell, Rudolf Virchow, Louis Pasteur, Joseph Lister, William Osler, Walter Reed, Sigmund Freud, Harvey Cushing, Alice Hamilton and Hans Zinsser. A brief chapter entitled The New Frontiers offers a brief glimpse into the work of more recent men, such as Paul Ehrlich and Sir Alexander Fleming. The reproductions and printing are commendable. There is a fairly complete index.

The Sociology of the Patient: A Textbook for Nurses. By Earl Lomon Koos, Ph.D., Professor and Chairman, Department of Sociology, University of Rochester, New York. Cloth. $3. Pp. 264, with illustrations. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1950.

As the author suggests, nursing has become much more than wheeling a dressing cart, giving injections or carrying bed pans, and there is growing recognition of the significant part nurses can play in the recovery of the patient. This book is an excellent contribution toward better understanding by nurses of the social and psychologic aspects that may be extremely strong forces in recovery from illness. Because nurses are no longer untutored handmaids, they are in a position to read this type of discussion with understanding and benefit.

Presented as a working tool and with much more emphasis on practice than theory, the volume employs various devices to indoctrinate the reader. Three different aspects are considered, the individual patient, the patient in relation to his family and other groups and the patient's interests and problems. At the end of each chapter are review questions and a bibliography, and at the end of each of the three sections are brief summaries interpreting the material just presented.

An appendix contains a glossary of terms the author feels may be sufficiently unfamiliar to warrant exact definition, a series of supplementary projects or investigations that may be carried out by the reader, an outline for studying the patient and his family, a list of visual aids and sources and an extensive reading list. Physicians can recommend this volume to nurses and office secretaries. It should be given serious consideration by all nurses' training school supervisors.

QUERIES AND MINOR NOTES

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted on request.

DETERMINATION OF VITAL LUNG CAPACITY

To the Editor:—Please discuss the determination of vital lung capacity, its use as a routine procedure in physical examinations in general practice.

Robert J. Ralston, M.D., Holyoke, Colo.

ANSWER.—Vital capacity is the amount of air which can be drawn into the lungs between forced expiration and inspiration. One makes the measurement by having the patient take as deep an inspiration as possible and then breathe out as much as possible, with the maximum volume of air expelled being recorded as the vital capacity. It is recommended that observations should be made under carefully standardized conditions to eliminate any possibility of results being affected by such factors as time of day, nearness to meals and body position. The patient should stand erect, in an easy relaxed posture, and the highest of several readings should be recorded. Varying body positions, fulness or emptiness of the stomach and muscular effort at the time of measurement may affect readings. To avoid unnecessary duplication of equipment it has been suggested that the physician employ a spirometer adaptable to determination of metabolic rate as well as vital capacity. Any condition which reduces the alveolar air spaces or restricts the movement of the diaphragm or thoracic wall will cause lowered readings. This includes intrathoracic tumors, pleural effusions or adhesions, paralysis of the thoracic or abdominal musculature, intra-abdominal tumors or effusions and skeletal deformities. Recovery from heart failure severe enough to cause pulmonary congestion can be gaged by gradual increase in vital capacity. The Council on Physical Medicine and Rehabilitation has recently accepted a convenient pocket size instrument for measuring vital capacity (J.A.M.A. **142**:565 [Feb. 25] 1950).

GLOSSODYNIA

To the Editor:—A male veteran aged 27 was a prisoner of war in the Philippines. He had beriberi and other nutritional deficiencies. About three years ago he had extensive dental work done. The present complaint, glossodynia with burning sensation of the tongue and mouth, dates back to the time of the dental restorations. Is there any type of galvanometer with which one could test and/or measure the current induced in the mouth as the result of dissimilar metals? Both the dentist and the patient are reluctant to have the dissimilar metallic restorations removed unless it is shown that the case is one of Lain's disease (burning and erosion caused by electrogalvanism due to dissimilar metallic restorations).

M. D., California.

ANSWER.—The problem is difficult. The symptoms could arise from a galvanic field, although this is not common. The wartime nutritional deficiencies could have left changes which now result in the symptoms. It is presumed that a deficiency, excessive irritation from food or smoking, a psychogenic cause or even a roughening of the dentures is not present. A metallic taste and salivation would favor a galvanic field as the cause.

A galvanometer can be used to show the difference in potential although it will not prove that the current is the cause of the symptoms. An RCA ohmist can be used; one may be available in a well equipped radio repair shop. A Hewlett Packard 410-A voltmeter is also suitable. A physics or biophysics laboratory may also have one of these devices. Two stainless steel electrodes are applied to the different metals, and a reading of 0.1 to 0.2 volt would be significant.

OSTEOPOROSIS

To the Editor:—What is the best treatment for osteoporosis? Does a patient usually have pain with osteoporosis?

George A. Bakke, M.D., Oakland, Calif.

ANSWER.—It is not stated what part of the body is affected by osteoporosis in this particular case. Generally osteoporosis is found in patients of middle age or over. Osteoporosis of the spine is found most often in women well beyond the climacteric, it is prolonged in duration and painful, and no specific treatment is known. The diet should be investigated and controlled so that it is well balanced and contains adequate calcium, for which milk is the best source. Calcium lactate and even hypodermic injections of calcium may be given, but there is little evidence that these help. If the spine is involved it is often necessary for the patient to wear a brace or a corset, although in elderly persons braces are poorly tolerated.

Osteoporosis of the knee, shoulder or certain other areas has been known to develop in those taking potassium thiocyanate for hypertension; in such cases it gradually disappears with withdrawal of the drug. Osteoporosis may follow, and may be exceedingly painful after, fixation of a leg in a cast for fracture of the ankle. For this, as soon as the fracture is healed, use to the point of toleration is indicated. Elastic bandaging for the swelling so often encountered, massage, whirlpool baths and other measures will help. Occasionally osteoporosis of a foot and ankle develops without apparent cause, although the patient may remember a slight bump or knock that caused no immediate disability. This type of osteoporosis is often particularly intractable and may last from a few months to one and a half years. Here again the treatment is use to the point of toleration along with the aforementioned physical therapy measures.

There is no specific treatment for osteoporosis. The etiology has for its background calcium metabolism, and that is not yet thoroughly understood.

WASSERMANN REACTION

To the Editor:—A married man, aged 57, was found to have a 2 plus Wassermann reaction. The reaction of another specimen of blood was 1 plus and of a third specimen, 2 plus. All the tests were done at the state hygienic laboratory. A course of penicillin therapy, 6,400,000 units, was given and another test made, which revealed a 1 plus Wassermann reaction. In 1943 the Wassermann reaction was negative. The patient is in the employ of a plant manufacturing wood pulp, using a sulfite process, and is exposed to sulfuric acid fumes. Would this exposure influence the Wassermann reaction? Is a reaction of 1 or 2 plus of any significance? What treatment is indicated?

Victor Marshall, M.D., Appleton, Wis.

ANSWER.—It is at least conceivable that exposure to sulfite fumes may elicit a false positive serologic reaction for syphilis. Some believe that tissue injury in any form may in certain persons elicit a false reaction. Perhaps Dr. R. A. Nelson Jr. of Johns Hopkins Hospital, Baltimore, would be willing to carry out a spirochetal immobilization test on a blood specimen of this patient, or Dr. Reuben L. Kahn of the University of Michigan Hospital, Ann Arbor, could perform a "verification" test. These tests may indicate whether the weakly positive serologic reaction given by the patient is associated with syphilis or is a false positive reaction.

INJURY IN REGION OF KIDNEY

To the Editor:—A man aged 54 received injury to the left kidney area of the back. I saw him about twenty hours afterward. He had severe pain in the left kidney area, frequent, painful passage of dark urine and profuse sweating. He was restless and slept little that night. The temperature was 98.6 F., the pulse rate 90, the respiratory rate 20 and the blood pressure 96 systolic and 68 diastolic. The conjunctiva was pale. There was exquisite tenderness over the left kidney. Examination revealed moderate enlargement of the prostate. A roentgenogram of the lumbar portion of the spine and the kidney areas revealed essentially normal conditions, except for a moderate degree of osteoarthritis, consistent with the man's age. The urine was dark and apparently bloody, with albumin (1 plus); microscopic examination showed 4 plus red blood cells and 20 to 30 white blood cells per high power field. Examination of the blood showed 3,100,000 red blood cells, 72 per cent hemoglobin and 18,100 white blood cells. The patient was treated with calcium gluconate injections, penicillin, sulfonamide drugs and sedation. Bleeding stopped and pain subsided. Three weeks after the accident, the urine contained only an occasional red blood cell and the patient was symptom free. What is the possibility that impairment in the function of this kidney may develop at a later date?

M.D., Tennessee.

ANSWER.—After any trauma to the kidney, an excretory urogram is safe and indicated. If made within the first seventy-two hours, it usually will show diminished or absent function but will be of little value in determining the presence of urinary extravasation. Therefore a retrograde pyelogram should be made early to detect extravasation or changes in the course or angulation of the ureter. If the retrograde pyelogram reveals normal conditions and there is no definite mass in the loin, conservative management is indicated. Evidence of

extravasation or hemorrhage about the kidney indicates laceration and the need for surgical intervention, usually about the third day (McKay, H. W., and others: *J. A. M. A.* 141: 575 [Oct. 29] 1949).

In the case cited the intravenous pyelographic studies are certainly indicated at this time, and if there is any question about the outline or function of the excretory system, cystoscopy, differential dye studies with phenolsulfonphthalein and retrograde urography should be performed. If the results are normal, the chances are that serious damage has not occurred. It would still be advisable to repeat the examinations within six months to a year, in order to detect late hydronephrosis, atrophy or formation of stone.

NUMBNESS OF BOTH FEET

To the Editor:—A man aged 60 with diabetes has persistent burning and numbness of both feet unrelieved by adequate control of his diabetes and medication. His present blood sugar level is 130 mg. per hundred cubic centimeters, and his urine is sugar free. He is receiving 20 units of protamine zinc insulin and 10 units of the regular insulin before breakfast daily. What could be done to relieve the condition of his feet?

M.D., New York.

ANSWER.—The persistent burning and numbness of the feet is probably due to diabetic neuropathy. In this condition, although the ultimate prognosis is usually good as far as subjective findings are concerned, it often takes weeks, months or years for recovery. Almost invariably if one studies in detail the history of such patients, one finds in the relatively recent past a long period of poor control of diabetes. Treatment consists in continuous painstaking control of the diabetic condition with a restricted though adequate diet and the use of appropriate doses of insulin. Although no dramatic effect may be expected, the use of large supplements of vitamin B is desirable and recently some workers have reported benefit following the intramuscular injection of 15 micrograms of vitamin B_{12} once or twice weekly for several weeks. Analgesics and other symptomatic medicaments may be necessary during the period of recovery. Causes for neuritis other than diabetes must be kept in mind and ruled out by appropriate studies. Although the burning of the feet will probably clear up in time, there may remain varying degrees of insensitiveness to pain and temperature so that such patient may have feet which are vulnerable to various types of trauma. It is characteristic of diabetic neuritis that the spinal fluid shows an increase in total protein without increase in cells. In a diabetic person aged 60, particularly if the diabetes is of long duration, one would expect to find a considerable degree of arteriosclerosis. It may be difficult to assay the role of neuritis and that of arteriosclerosis in the pain, burning and numbness of the extremities.

MULTIPLE PROSTATIC CALCULI

To the Editor:—A patient has multiple calculi in the prostate, that protrude into the bladder. Sometimes he passes small calculi with bloody urine. What is the best diet to prevent formation of more calculi and perhaps to dissolve or favor the loosening and passing of those that are present. Should his urine be kept acid, alkaline or neutral?

M.D., New York.

ANSWER.—If the patient has true endogenous prostatic calculi, there is no way of preventing their formation or of causing their solution by diet or irrigation of the bladder. The only effective treatment is prostatectomy, but this must be a subtotal peritoneal prostatectomy to remove the prostate and its capsule together. This operation should be reserved for patients who have severe infection, urinary obstruction or suspected malignant lesions. It may produce impotence and is therefore indicated chiefly in the older age groups. Transurethral resection or punch operation may be used for temporary relief in young persons, but some of the calculi are usually not removed with these procedures.

LONG-CONTINUED ALBUMINURIA

To the Editor:—A patient aged 57 has had albuminuria for thirty-five years (varying from a trace to 2 plus). Specific gravity exceeds 1.020, and a few casts are now present. He is in good health, has normal blood pressure and no rise in the nonprotein nitrogen level. What is the prognosis? Would a salt free or low sodium diet or modified rice diet improve the outlook?

M. D., Canada.

ANSWER.—In view of the long duration of albuminuria without apparent change in renal function or blood pressure, there is no reason to worry about it at this time, nor is any specific dietary treatment indicated. It would be interesting to have an intravenous pyelogram of this patient made to exclude some congenital anomaly.

SPURS ON HEELS

To the Editor:—I have a patient with spurs on both heels. What treatment is recommended?

Blake S. Allison, M.D., Long Beach, Calif.

ANSWER.—A patient may have spurs of the heel without symptoms. Usually the spur is not the cause of pain or disability. It is nature's reaction to inflammation in this area. The inflammation is due to tension at the attachment of the plantar fascia, which is fan-shaped, wide in front and narrowed at the attachment to the os calcis. When the longitudinal arch is lowered the plantar fascia is unduly stretched and tension is concentrated at the calcaneal attachment. Continuous or repeated tension results in an inflammatory reaction which causes the pain and tenderness in this area. Treatment should be directed toward getting rid of the inflammation, relieving the tension and ultimately reestablishing the normal position of the foot. This would mean the treatment of pes valgo planus. To begin with, the heel may be brought into a varus position by means of adhesive strapping. In the exceedingly acute phase heat and rest should precede the strapping. After one completes the strapping, correction should be taken by means of corrective shoes such as those described by E. D. W. Hauser (Diseases of the Foot, ed. 2, Philadelphia, W. B. Saunders Company, 1950, chap. 5). It is possible to relieve the tension on the plantar fascia by a surgical procedure in which the entire calcaneal attachment is freed and the spur and inflammatory tissue are removed. This gives more rapid relief of the pain, but it may take longer to reestablish the normal position of the foot. Sometimes the spur is so large and so placed that it causes irritation and must be removed.

DETERMINATION OF PROTHROMBIN TIME

To the Editor:—An inquiry on the determination of prothrombin time appeared in *The Journal* April 15, page 1254. The answer was satisfactory in some respects, but it does not, I believe, adequately reflect the experience of all groups of workers. I am particularly concerned about the statement "The best preparation is one which will give a prothrombin time with normal plasma under 15 seconds, preferably 11 to 12.5 seconds." This is not in agreement with my experience. The query refers to a preparation advertised in *The Journal* which appears to be the commercial lung thromboplastin marketed by Chilcott Laboratories, division of the Maltine Company. Associates and I have recommended this product in our publications, and in practically all of our studies made in the past five or six years we have employed this preparation, which yields average normal prothrombin times of 15 ± 1.5 seconds and 39.5 ± 2.5 seconds on whole and diluted (12.5 per cent) plasma respectively (Shapiro, S., and Weiner, M.: Coagulation, Thrombosis and Dicumarol, New York, Brooklyn Medical Press 1949). Other workers with wide experience in the field of dicumarol® therapy have reported practically identical values. Thus, Foley and Wright (*Am. J. M. Sc.* 217: 136 [Feb.] 1949) give 15 ± 1 seconds for whole plasma and 38 ± 3 seconds for diluted (12.5 per cent) plasma. These authors discard any thromboplastin with values outside these limits. The standards reported by Overman, Newman and Wright (*Am. Heart J.* 39: 156 [Jan.] 1950) in 828 estimations on normal plasmas using rabbit lung thromboplastin were the same, their mean being 15.8 ± 1.2 seconds for whole plasma.

The most satisfactory thromboplastin is one which will reflect with the most accuracy the extent of the accelerated clotting time. One of the reasons we establish normal values of both whole and diluted (12.5 per cent) plasma prothrombin time is to determine the sensitivity of the thromboplastin in detecting hypoprothrombinemia especially after dicumarol® therapy and in liver disease and hyperprothrombinemia when it occurs clinically, as in thrombotic disorders and in liver disease. It has been our experience that thromboplastin which exhibits the characteristics which we advocate and which are previously described reflects prothrombin response both in the range of hypoprothrombinemia and hyperprothrombinemia more reliably than those which give normal values in the whole or diluted (12.5 per cent) plasma outside these limits. Thromboplastin with normal values less than these, in our hands, failed to reflect adequately the extent of dicumarol®-induced hypoprothrombinemia. An example of this is Russell viper venom (stypvin), which has been found responsible for hemorrhagic complications as reported by Wilson (*Proc. Soc. Exper. Biol. & Med.* 66: 126 [Oct.] 1947), Biggs and Macfarlane (*J. Clin. Path.* 2: 33, 1949) and James (*J. Clin. Path.* 2: 45, 1949). Thromboplastin of lesser activity yields normal values beyond this range and may show a false and exaggerated response; hence, it might be responsible for a dosage level of dicumarol® insufficient for therapeutic effect. It seems only realistic to point out that different workers in a rapidly advancing field may have different concepts, methods and standards. For example, in contrast with the results previously referred to and the published reply to Dr. McVeagh, a range of 15.4 to 18.4 seconds for whole plasma of 93 normal subjects was reported by Martin, Curfman and Cavano (*J. Lab. & Clin. Med.* 32: 554 [May] 1947). It is confusing to the clinician using dicumarol® therapy to be given fixed standards by one group of workers which are not accepted by others. I believe the rigid limits established in the answer to this question should be modified; that we recognize that other outstanding clinics are successfully carrying out dicumarol® treatment with the aid of thromboplastin, commercial or self prepared, giving times with an over-all range of 11 to 18 seconds but with specific limits established by the experience of each group.

Shepard Shapiro, M.D., New York 28.